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IN THE

Supreme Court of the United States

OCTOBER TERM, 1984

BRISTOL-MYERS COMPANY,

Petitioner,

—v.—

FEDERAL TRADE COMMISSION,

Respondent.

PETITION FOR WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SECOND CIRCUIT

APPENDIX

KENNETH A. PLEVAN
(Counsel of Record)
MIRIAM L. SIROKY
ELAINE D. ZIFF
SKADDEN, ARPS, SLATE,
MEAGHER & FLOM
919 Third Avenue
New York, New York 10022
Tel: (212) 371-6000

GILBERT H. WEIL
(Counsel of Record)
GERALD GUTTMAN
JAY S. DAVIS
WEIL, GUTTMAN, DAVIS
& MALKIN
60 East 42nd Street
New York, New York 10165
Tel: (212) 687-8573

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UNITED STATES COURT OF APPEALS

FOR THE SECOND CIRCUIT

No. 1053—August Term, 1983

(Argued April 2, 1984 Decided June 25, 1984)

Docket No. 83-4167

BRISTOL-MYERS COMPANY,

Petitioner,

—v.—

FEDERAL TRADE COMMISSION,

Respondent.

Before:

FEINBERG, *Chief Judge*,
FRIENDLY and OAKES, *Circuit Judges*.

Petition seeking review of an order of the Federal Trade Commission which required that petitioner cease and desist various deceptive advertisements for a number of its drug products, particularly its over-the-counter analgesics, Bufferin and Excedrin.

Order enforced.

KENNETH A. PLEVAN, New York, N.Y. (Miriam L. Siroky, Elaine D. Ziff, Skadden, Arps, Slate, Meagher & Flom, New York, N.Y.; Gilbert H. Weil, Gerald Guttman, Jay S. Davis, Weil, Guttman, Davis & Malkin, New York, N.Y., of counsel), *for Petitioner.*

MELVIN H. ORLANS, Attorney, Federal Trade Commission, Washington, D.C. (John H. Carley, General Counsel, Howard E. Shapiro, Deputy General Counsel, Ernest J. Isenstadt, Assistant General Counsel, Federal Trade Commission, Washington, D.C., of counsel), *for Respondent.*

OAKES, *Circuit Judge*:

Bristol-Myers Company (Bristol) petitions for review of an order of the Federal Trade Commission (the Commission or FTC) made in respect to the advertising by Bristol of its well-known analgesics, Bufferin and Excedrin. The order represents over ten years of agency work formally commencing with the filing of complaints on February 23, 1973 by the Commission against Bristol and its advertising agencies, Ted Bates & Co., Inc. and Young & Rubicam, Inc., concerning alleged violations of sections 5 and 12 of the FTC Act, 15 U.S.C. §§ 45 and 52 (1982). On the same day the Commission also filed complaints challenging the advertising of certain competing non-prescription internal analgesic products, including Anacin (*In re American Home Products Corp.*, 98 F.T.C. 136,

362 (1981), *enforced as modified, American Home Products Corp. v. FTC*, 695 F.2d 681 (3d Cir. 1983) (*AHP*)[1]), and Bayer Aspirin (*In re Sterling Drug, Inc.*, No. 8919 (July 5, 1983), *appeal pending*, No. 83-7700 (9th Cir. filed Jan. 30, 1984)). We have considered each of Bristol's claims as to the remedial order and deny the petition for review and grant enforcement.

The Commission Decision and Order

The Commission's decision upheld findings by its Administrative Law Judge (ALJ) that Bristol had engaged in a variety of deceptive practices in advertising Excedrin and Bufferin from 1960 to 1973, but dismissed the complaint allegations concerning Excedrin PM because it found that Bristol had not made the challenged claims as to that product. In concluding that Bristol and its advertising agencies had deceptively advertised Excedrin and Bufferin, the Commission found that Bristol had misrepresented that the analgesic superiority of Excedrin and Bufferin over competing products was scientifically proved, or "established," by the artful use of certain phrases such as "scientific tests" and "medically endorsed," as well as by the use of visual images. Bristol was found to have made seven false and deceptive claims of this nature, concerning both the efficacy and the freedom-from-side-effects of its non-prescription internal analgesic products.[2] Part I of the Order prohibits Bristol

1 Following the Third Circuit's decision in *AHP*, the FTC reopened its proceedings against AHP and subsequently modified the order to make it similar in scope to the orders in *Bristol* and in *Sterling Drug*. *See In re American Home Products Corp.*, No. 8918, June 7, 1984.

2 Such claims that the efficacy or safety of a product is scientifically established will be referred to as "establishment claims," and the non-prescription internal analgesics at issue here will be referred to as

from making comparative establishment claims asserting the superior effectiveness or freedom-from-side-effects of its OTC internal analgesics without proof consisting of "two or more adequate and well-controlled clinical investigations" conducted in accordance with procedures set forth in detail in the Order.

In addition the Commission found that Bristol had claimed, without a reasonable basis, that both Bufferin, which is a form of buffered aspirin, and Excedrin, a combination of aspirin, salicylamide, acetaminophen and caffeine, relieved tension and that physicians recommend Bufferin more frequently than they recommend any other OTC internal analgesic. Finding that such unsubstantiated claims were deceptive, the Commission in Part II of its Order requires Bristol not to make "any therapeutic performance or freedom-from-side-effects claim" for any OTC internal analgesic unless it has a "reasonable basis for making that claim [consisting of] competent and reliable scientific evidence supporting that claim." Part II, then, requires that all claims of this type be reasonable, while Part I imposes more rigorous requirements on similar comparative establishment claims.

The Commission also found that Bristol deceptively advertised that its products contained "unusual" or "spe-

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"OTC" (over the counter) internal analgesics. Further, we adopt the Commission's use of the term "comparative claim" to mean a claim which compares one drug with another, with "noncomparative claim" being a claim made uniquely about one product.

Bristol misrepresented that it had been established that: (1) Bufferin relieves pain faster than aspirin; (2) Bufferin relieves pain twice as fast as aspirin; (3) Bufferin will upset a person's stomach less frequently than aspirin; (4) a dose of Excedrin relieves more pain than a dose of aspirin; (5) a dose of Excedrin relieves twice as much pain as a dose of aspirin; (6) Excedrin is a more effective pain reliever than aspirin or any other OTC analgesic; and (7) Excedrin is more effective than any other OTC analgesic because it has four ingredients. Charges that Bristol had made eight other establishment claims were dismissed, because the claims were found not to have been made.

cial" ingredients even though the very same ingredients are commonly used in other OTC drug products intended for the same use or uses as the product advertised. These "special ingredient" claims were also found to have been made so as to conceal the fact that Bufferin and Excedrin were aspirin based, the deception operating by way of emphasis upon the unspecified analgesic ingredient. Part IIIA of the Order prohibits special ingredient advertising when the ingredient referred to is commonly used in other products for the same purpose. Noting that Bristol had previously signed stipulations in respect to special ingredient claims for a cold remedy and a facial cream, this part of the Order was applied across the board to all Bristol OTC products and not merely to OTC internal analgesics.

The Commission further found that Bristol falsely represented that doctors recommend Bufferin more than any other OTC internal analgesic. Part IIIB of the Order prohibits Bristol from representing "that any group, body or organization endorses or recommends [the use of a Bristol OTC drug] unless at the time such statement or representation is made, respondent has a reasonable basis for such statement or representation." This part of the Order was applied to all Bristol OTC drug products in the light of an earlier history of similar "doctors recommend" claims made by Bristol in connection with other products. *See In re Bristol-Myers Co.*, 46 F.T.C. 162, 170 (1949) (order), *aff'd*, 185 F.2d 58 (4th Cir. 1950); 24 F.T.C. 1554 (1937) (stipulation).

On the other hand, the Commission declined to accept complaint counsel's recommendation that Bristol be required to run corrective advertising. *See Warner-Lambert Co. v. FTC*, 562 F.2d 749, 756-59 (D.C. Cir. 1977), *cert. denied*, 435 U.S. 950, 98 S.Ct. 1576, 55 L.Ed.2d 800 (1978). It also declined to uphold the ALJ insofar as his

order would have applied to the labelling of Bristol products as well as to Bristol's advertising, in the light of the FTC's liaison agreement with the FDA as set forth in *AHP*, 98 F.T.C. at 411.

Discussion

Bristol makes a variety of objections to all three parts of the Order. As to Part I, Bristol contends that it should apply only to effectiveness claims, and that it should permit reliance on FDA studies. Part II is alleged to be unduly and unconstitutionally vague and overbroad, and is also said to rely on an "advertising substantiation" doctrine which violates the First Amendment. Part III is also allegedly overbroad. Moreover Part IIIA is said not to be reasonably related to any violation actually found by the FTC, and Part IIIB based upon fact-finding which is clearly erroneous.[3]

A. *Part I's applicability to freedom-from-side-effects claims*. Bristol argues that the FTC had no basis for requiring two adequate, well-controlled clinical studies for freedom-from-side-effects comparative claims, so that Part I of the Order should be modified to apply solely to effectiveness claims. The Commission is said to have relied in formulating the two studies requirement upon FDA regulations which themselves distinguish between effectiveness claims, the validity of which should be

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3 On appeal Bristol argued that Part II's reasonable basis requirement for noncomparative claims put it at a disadvantage in relation to AHP, since the Third Circuit deleted the reasonable basis provision from the FTC's order in *AHP*. However, when the Commission modified the order in *AHP* in light of the Third Circuit's opinion, it included a new reasonable basis provision analogous to the one we are addressing here designed to meet the objections of the Third Circuit in *AHP*. Thus Bristol's competitive disadvantage argument has been mooted by the modified order in *AHP*.

proved by "controlled clinical investigations," and safety claims, proof of which "shall consist of adequate tests by methods reasonably applicable. . . ." 21 C.F.R. § 330.10(a)(4)(i) (safety), (ii) (effectiveness) (1983). The Commission is also said to have erred in stating that its clinical study requirement is consistent with the 1962 amendments to the Food, Drug and Cosmetic Act of 1938, 21 U.S.C. § 355(d) (1982). Under that statute, Bristol states, the "substantial evidence standard" applies only to product effectiveness claims and does not apply to safety claims. *See E.R. Squibb & Sons, Inc. v. Weinberger*, 483 F.2d 1382, 1385 (3d Cir. 1973). And pointing to the Commission's own opinion in *AHP*, Bristol notes that no freedom-from-side-effects claims were held subject to the two well-controlled clinical studies requirement in *AHP*. This is so because the only freedom-from-side-effects establishment allegation made in that case was dismissed because AHP was found not to have made the claim. 98 F.T.C. at 374 n.21. Bristol proposes that the correct test should be that product safety may be evaluated by "clinical or other experience, tests, or other scientific data." *See E.R. Squibb & Sons*, 483 F.2d at 1385 nn.18, 19. Under that standard Bristol states that it submitted four studies to support its claim that Bufferin upsets the stomach less frequently than aspirin.

We agree with the Commission, however, that the side-effects portion of Part I is premised on the Commission's factual determination supported by substantial evidence, that only two well-controlled clinical studies could establish Bristol's superior freedom-from-side-effects claim for Bufferin. Even assuming that Bristol is entitled to raise this question here for the first time, *United States v. L.A. Tucker Trucklines, Inc.*, 344 U.S. 33, 36-37, 73 S.Ct. 67, 68-69, 97 L.Ed. 54 (1952), the Commission

found that Bristol claimed that Bufferin was proven to cause less stomach upset than aspirin without adequate substantiation. Dr. Grossman, an expert in the field of gastroenterology and gastrointestinal side-effects of aspirin, testified that only well-controlled clinical studies could establish that Bufferin causes less stomach upset than aspirin. His testimony amounts to substantial evidence on the record, which the Commission was entitled to rely upon in setting its standard. It should also be noted that the Third Circuit, in the context of reviewing the "substantial question" doctrine in that case,[4] concluded that both comparative safety (freedom-from-side-effects) and comparative effectiveness claims could appropriately be subjected to the two clinical test standard. *See* 695 F.2d at 695-98. Here as there the Order is upheld as supported by substantial evidence.

Insofar as FDA requirements and regulations are concerned, they simply do not govern this case. Not only is a different regulatory scheme involved, but generally speaking the FDA is concerned only with evaluating absolute safety and efficacy, and not with the questions of comparative safety and efficacy that arise in OTC drug advertising. Moreover, *E.R. Squibb & Sons*, 483 F.2d 1382, is wholly inapposite. That case involved withdrawal, not approval of a new drug application, and in providing that withdrawal may take place where "clinical or other experience, tests, or other scientific data show that such drug is unsafe," 21 U.S.C. § 355(e)(1) (1982),

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4 In *AHP*, Part I-B of the Commission Order provided that whenever AHP's advertisements claim superior effectiveness or freedom-from-side-effects, even when those advertisements do not overtly claim that this superiority has been established or proven, AHP must provide two or more well-controlled clinical studies to support the superiority claims or disclose that the superiority is open to "substantial question." *See* 695 F.2d at 684, 693-702. The "substantial question" provision of the *AHP* order was subsequently dropped from the modified order.

the FDA regulatory scheme simply provides a low threshold for withdrawal of a drug on safety grounds.

B. *Part I and FDA approval as establishment evidence.* Bristol seeks to modify Part I of the Commission Order to permit it to rely upon FDA regulations or other definitive FDA action approving claims for OTC internal analgesics as "establishing" such claims. Since the FDA is responsible under its Act, 21 U.S.C. §§ 301-392 (1982), to ensure that all OTC drugs are safe, effective and not misbranded, *see* 21 C.F.R. § 330.10 (1983), Bristol argues that the FTC should be satisfied by FDA approval. In this connection we note the existence of a liaison agreement between the two agencies, 36 Fed. Reg. 18,539 (1971), whereby the FTC defers to the FDA when allegedly deceptive claims appear on labelling for food, drugs or cosmetics. And we also note that the FDA has instituted an OTC Drug Review Program. *See* 21 C.F.R. § 330.1 (1983); *see generally Cutler v. Kennedy*, 475 F. Supp. 838, 844-45 (D.D.C. 1979).

Here too Bristol's contentions could be rejected on the ground that they were not previously raised before the Commission. Even on the merits, however, the modifications Bristol requests are unnecessary, if not undesirable. As we have indicated, the FDA's regulations are concerned almost exclusively with absolute claims. Part I of the Commission's Order here deals solely with comparative establishment claims. Therefore almost nothing would be gained by allowing the FDA's regulations to be used as requested by Bristol. Moreover FDA determinations are usually complex and subject to varying interpretations. To allow Bristol to rely on its evaluation of these determinations could conceivably lead to more deceptive advertisements and to more disputes with the FTC. The Commission is entitled to fashion its order to avoid such

problems. There is nothing, however, to prevent Bristol from seeking modification from the Commission under section 5(b) of the Act, 15 U.S.C. § 45(b) (1982), and Commission regulations, 16 C.F.R. § 3.72 (1984) in the unlikely event that the FDA has occasion to consider a particular relevant comparative establishment claim and approves it without clinical testing.

C. *Part II's alleged vagueness.* Citing *FTC v. Colgate-Palmolive Co.*, 380 U.S. 374, 392, 85 S.Ct. 1035, 1046, 13 L.Ed.2d 904 (1965), Bristol argues that Part II of the Order is unduly vague insofar as it declines to specify "the amount and kinds of evidence necessary to constitute a reasonable basis for Bristol-Myers' future claims." The Commission has allegedly improperly left the determination of what constitutes a reasonable basis to case-by-case analysis. This is especially unfair, Bristol argues, because the only reasonable basis violation found in this case relates to a discontinued claim by Bristol that Excedrin, a drug containing caffeine as one ingredient, is a "tension reliever." Finally, Bristol points to the Third Circuit's statement in *AHP* that "[b]ecause the Commission has chosen not to bind itself in advance to rules as to the interpretation of the phrase 'reasonable basis,' any order which essentially relies upon 'reasonable basis' language will be imprecise, although not necessarily so." 695 F.2d at 710.

But absolute precision is not possible in certain FTC orders, and we have upheld reasonable basis provisions formulated in substantially identical terms. *E.g.*, *Jay Norris, Inc. v. FTC*, 598 F.2d 1244, 1245-46, 1250-51 (2d Cir.), *cert. denied*, 444 U.S. 980, 100 S.Ct. 481, 62 L.Ed.2d 406 (1979); *see also* our decision enforcing the FTC's order in *In re Fedders Corp.*, 85 F.T.C. 38, 69 (1975) (performance claims for airconditioners must be

substantiated by "competent scientific, engineering or other similar objective material"), *order enforced, Fedders Corp. v. FTC*, 529 F.2d 1398 (2d Cir.), *cert. denied*, 429 U.S. 818, 97 S.Ct. 63, 50 L.Ed.2d 79 (1976). We note also that Part II of the Order is limited in scope to performance and side-effects claims for OTC internal analgesics and that it defines reasonable basis to consist of "competent and reliable scientific evidence." Moreover, the Commission has issued some 21 litigated orders and 126 consent orders involving advertising substantiation using equivalent language. If the Third Circuit decision in *AHP* may be read as holding that the reasonable basis standard of "competent and reliable scientific evidence" is excessively vague, with respect we decline to follow it since our own decisions require that we uphold the Order. But we note that the *AHP* court recognized that while reasonable basis language is "imprecise," it was careful to add the clause, "although not necessarily fatally so." 695 F.2d at 710. The part of the Order in that case was in fact vacated for the combined problems of overbreadth and vagueness.

D. *Part II's alleged overbreadth and unreasonable relation to the violation.* Every provision of the Order must bear a "reasonable relation" to the conduct of Bristol that was found unlawful. *See ITT Continental Baking Co. v. FTC*, 532 F.2d 207, 220-21 (2d Cir. 1976). Part II of the Order prohibits unsubstantiated claims concerning effectiveness and freedom-from-side-effects. Bristol argues that the only effectiveness claim it made that was found to be without a reasonable basis was the noncomparative claim that Bufferin and Excedrin relieved tension, and that this finding is too narrow a basis to justify Part II of the Order. The Third Circuit, in striking the "reasonable basis" provision in Part II-D of

the *AHP* Order as vague and overbroad, did so in part because the only noncomparative advertising claim on which that part of the Order was based was the claim that Anacin relieves tension. 695 F.2d at 711.

But we agree with the Commission that Part II of the Order here is more narrowly drawn than the section struck in *AHP*. The provision is limited to the product category in question, namely OTC internal analgesics, and directly addresses that violation. Moreover, none of the violations covered by Part II are also covered by other parts of the Order. In the original *AHP* order nonestablishment comparative claims were covered by a separate "substantial question" provision. Bristol's advertising of this nature is pervasive, involving two different OTC internal analgesic products and encompassing widely disseminated comparative and noncomparative claims regarding both performance and freedom-from-side-effects.

Under the "fencing-in" doctrine, the Commission may frame a remedy which extends beyond the precise illegal conduct found. *See FTC v. Colgate-Palmolive Co.*, 380 U.S. 374, 395, 85 S.Ct. 1035, 1048, 13 L.Ed.2d 904 (1965); *FTC v. National Lead Co.*, 352 U.S. 419, 428-29, 77 S.Ct. 502, 508-09, 1 L.Ed.2d 438 (1957). Considering the nature and extent of the violation, the adaptability or transferability of the practice to other products and the past record of performance, the factors considered by the Ninth Circuit in *Sears, Roebuck & Co. v. FTC*, 676 F.2d 385 (9th Cir. 1982), the Commission's Order must be supported here. From 1960 to 1973, Bristol spent over two hundred fifty million dollars advertising its products, and in the process it made seven deceptive establishment claims and three deceptive reasonable basis claims. In sum we find it proper for the Commission to rely on false

establishment claims as a basis for extending the Order's coverage to deceptive nonestablishment claims. *See Porter & Dietsch, Inc. v. FTC*, 605 F.2d 294, 305-06 (7th Cir. 1979), *cert. denied*, 445 U.S. 950, 100 S.Ct. 1597, 63 L.Ed.2d 784 (1980); *In re Firestone Tire & Rubber Co.*, 81 F.T.C. 398, 441, 462-63 (1973), *order enforced, Firestone Tire & Rubber Co. v. FTC*, 481 F.2d 246 (6th Cir.), *cert. denied*, 414 U.S. 1112, 94 S.Ct. 841, 38 L.Ed.2d 739 (1973). To rule otherwise would allow Bristol to continue to make the same unsubstantiated and false claims by simply removing the "doctors recommend" language from its advertisements.

Bristol argues, moreover, that the FTC never considered whether Bristol had a reasonable basis for its establishment claims in this case since they were covered by the more rigorous standard of Part I of the Order. But this is beside the point when we consider the number of establishment claims that were in fact proven unsubstantiated. In terms of the history of Bristol's dealings with the Commission,[5] while Bristol prevailed in *In re Bristol-Myers Co.*, 85 F.T.C. 688, 741, 743 (1975), and received only a warning in *In re Bristol-Myers Co.*, 74 F.T.C. 780, 851, 860 (1968) (violation found but no order entered), we note that Bristol has entered into seven stipulations admitting violations charged which may be introduced into

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5 For litigated cases involving Bristol, *see In re Bristol-Myers Co.*, 36 F.T.C. 707, 715 (1943) (false and deceptive advertising claims regarding the laxative "Sal Hepatica"); *In re Bristol-Myers Co.*, 46 F.T.C. 162, 170 (1949) (false therapeutic claim for "Ipana" toothpaste and false claim that dentists recommend it), *aff'd*, *Bristol-Myers Co. v. FTC*, 185 F.2d 58 (4th Cir. 1950); *In re Grove Laboratories*, 71 F.T.C. 822, 830 (1967) (false and deceptive advertisements regarding "Pazo Formula," a hemorrhoid preparation), *enforced in part*, *Grove Laboratories v. FTC*, 418 F.2d 489 (5th Cir. 1969); *In re Bristol-Myers Co.*, 74 F.T.C. 780, 851, 860 (1968).

evidence in any subsequent proceeding.[6] Bristol's repeated use of false and misleading advertising amply justifies the scope of Part II of the FTC's remedial order.

E. *The First Amendment Argument.* Bristol argues that Part II violates the First Amendment in the light of the protection due commercial speech. *See Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 96 S.Ct. 1817, 48 L.Ed.2d 346 (1976). *See also In re RMJ*, 455 U.S. 191, 207, 102 S.Ct. 929, 939, 71 L.Ed.2d 64 (1982). But, as we have pointed out, deceptive advertising enjoys no constitutional protection and it may be regulated, *Jay Norris*, 598 F.2d at 1251-52; *see In re RMJ*, 455 U.S. at 203, 102 S.Ct. at 937. Even in the absence of a finding of actual deception, agencies may properly regulate speech that is merely potentially deceptive. *See Friedman v. Rogers*, 440 U.S. 1, 15, 99 S.Ct. 887, 897, 59 L.Ed.2d 100 (1979). This Order is not as broad as the order we upheld against First Amendment challenge in *Jay Norris*.

Nor is the prior substantiation doctrine as applied here in violation of the First Amendment. Bristol contends that the FTC is not entitled to presume that consumers

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6 The stipulations are as follows:

24 F.T.C. 1546 (1937) (health claims regarding "Vitalis" hair oil); 24 F.T.C. 1554 (1937) (health claims regarding "Ipana" toothpaste); 24 F.T.C. 1558 (1937) (health claims regarding the laxative "Sal Hepatica"); 25 F.T.C. 1626 (1937) (health claims for an alleged cold remedy, "Minit-Rub"); 27 F.T.C. 1602 (1938) (false claims for "Ingram's Milkweed Cream"); 27 F.T.C. 1609 (1938) (health claims for "Ingram's Shaving Cream"); *In re Bristol-Myers Co.*, 47 F.T.C. 1441 (1950) (complaint dismissed and stipulation accepted regarding an alleged cold remedy, "Resistab").

These stipulations, like consent orders, provide that they do not constitute admissions of violations, *see ITT Continental Baking Co. v. FTC*, 532 F.2d 207, 222-23 n.23 (2d Cir. 1976); 3 Trade Reg. Rep. (CCH) ¶ 9593, at 17,095. The stipulations, however, contain a clause authorizing the Commission to use the stipulated facts as evidence in subsequent proceedings against the party. *See, e.g.*, 24 F.T.C. 1405, 1405 n.2 (stipulation clause).

expect all supportable product claims to possess a reasonable basis to support the claims. It therefore wishes us to reject a whole series of FTC cases allegedly relying on such a presumption. *See, e.g., In re National Commission on Egg Nutrition*, 88 F.T.C. 84, 174, 191 (1976), *enforced as modified, National Commission on Egg Nutrition v. FTC*, 570 F.2d 157 (7th Cir. 1977).

Whatever the merits the argument that the use of such a presumption violates the First Amendment, it is clear that in this case the FTC made a factual finding, based on its investigation of Bristol's ads, that consumers viewing the ads would believe them to be making claims supported by a reasonable basis. It then found that lacking such a basis the ads were deceptive. A conclusion of this nature is "in the very realm of the Commission's greatest expertise—what constitutes deception in advertising. . . . As such the reviewing court must give the Commission's findings 'great weight.' " *Fedders Corp. v. FTC*, 529 F.2d 1398, 1403 (2d Cir.) (citations omitted), *cert. denied*, 429 U.S. 818, 97 S.Ct. 63, 50 L.Ed.2d 79 (1976). We find the conclusion amply supported in this case.

F. *Part IIIA of the Order and its relation to finding of a violation.* Bristol argues that Part IIIA, which applies to "unusual or special ingredient representations" for all of its OTC drugs, does not relate to any violations found to have been committed by it, since the corresponding allegations in the complaint were resolved in favor of Bristol. A Commission order purporting to "remedy wrongs which the Commission found not to have been committed" should be set aside, *ITT Continental Baking Co. v. FTC*, 532 F.2d at 221. Bristol refers to the fact that the Commission reversed the ALJ's finding that it had represented that Excedrin PM "contains a special sedative or sleep-inducing agent available only in Excedrin PM"

whereas that ingredient was available in other OTC drugs as well.

But we agree with the Commission that Part IIIA is reasonably related to the violation made by misrepresenting that Bufferin and Excedrin do not contain aspirin. The Commission specifically found that one of the ways Bristol had hidden the aspirin content of its products was by "falsely represent[ing] that Bufferin and Excedrin contained special or unusual ingredients." That finding is concededly supported by substantial evidence in that some of Bristol's advertising included the statements that Excedrin contains a pain reliever which works better than "common aspirin" or "plain aspirin" or that it contains "four medically-endorsed ingredients" providing special benefits. We note that AHP has a similar order imposed as proper "fencing-in," *see* 695 F.2d at 702.

G. *The Finding underlying Part IIIB.* Bristol advertised for a time that doctors recommended Bufferin more than any other "leading brand" of OTC internal analgesic. Bristol argues that Part IIIB of the Order, which enjoins Bristol from representing without a reasonable basis that any group endorses or recommends any OTC drug, was based upon a finding that those "doctors recommend" claims for Bufferin were made without appropriate prior substantiation. This finding is said to be without support, Bristol claims, since Bufferin *was* recommended by doctors more often than any other "leading brand" of OTC internal analgesic, a claim which was supported by the National Disease and Therapeutic Index. The FTC agrees that from 1967 through 1971 doctors recommended Bufferin more than Bayer, Excedrin and Anacin. However the Commission found that the ads conveyed the message that physicians recommend

Bufferin more than any other OTC internal analgesic, and not just the three other leading brands of aspirin-based products. Since in fact doctors recommend Tylenol, Ascriptin and generic aspirin more often than Bufferin, the FTC found the message conveyed by the ads false and misleading. *See AHP*, 695 F.2d at 687 & n.10; *FTC v. Sterling Drug, Inc.*, 317 F.2d 669, 674 (2d Cir. 1963); *see also Donaldson v. Read Magazine, Inc.*, 333 U.S. 178, 188, 68 S.Ct. 591, 597, 92 L.Ed. 628 (1948).

In interpreting advertisements the Commission may rely on its own expertise in this area and need not resort to surveys and consumer testimony, *J.B. Williams Co. v. FTC*, 381 F.2d 884, 890 (6th Cir. 1967). In this case the FTC's finding that the ads indicate that doctors recommend Bufferin more than any other OTC internal analgesic is clearly supported by substantial evidence on the record. The video portion of the Bristol advertisement unqualifiedly and explicitly says "doctors specify Bufferin most," which would plainly be understood to mean that Bufferin was preferred to all other OTC internal analgesics. The fact that the audio was qualified by the reference to "all leading brands of pain reliever" does not take the effect on the consumer of the full ad into account. *See Continental Wax Corp. v. FTC*, 330 F.2d 475, 477 (2d Cir. 1964).

H. *Part III's application to all nonprescription drugs.* It is argued that Part III of the Order, which limits special ingredients claims and imposes a reasonable basis requirement for "doctors prescribe most" claims made on behalf of *all* of Bristol's OTC drugs, constitutes improper "fencing-in" and so imposes an unreasonable compliance burden on Bristol. Bristol markets sixty categories of OTC products, including antiperspirants, cough

and cold remedies, hemorrhoid medication, laxatives, skin protectants, sunburn prevention products, antiseptic lotions and others. *See Standard Oil Co. of California v. FTC*, 577 F.2d 653 (9th Cir. 1978) (striking down multi-product order). The Third Circuit rejected, however, a similar argument in *AHP*, 695 F.2d at 704-06, distinguishing *Standard Oil*, where on the strength of just three implicitly misleading advertisements for a single product, a manufacturer and its advertising agency were subjected to an order covering thousands of products, 577 F.2d at 661. Here as in *AHP*, we believe it is appropriate "fencing-in" to extend the product coverage to other Bristol OTC drugs.

Bristol argues under *Sears, Roebuck*, 676 F.2d at 392, that the extent of the alleged violations, the transferability of the violations to other contexts, its limited past history of deceptive advertising, and other considerations, including vigorous competition from nonaspirin analgesics, all go to make Part III of the Order invalid as constituting too extensive "fencing-in." However, the coverage of Part III is quite narrow, being limited in IIIA to false claims that an ingredient is unusual or special and in IIIB to unsubstantiated claims regarding recommendations or endorsements.

Moreover, most of the facts which we found justified the "fencing-in" in Part II of the Order also justify the "fencing-in" in Part III. To summarize briefly these findings: the violations were extensive; it would be easy to make other similar false special ingredient or unsubstantiated recommendation claims as regards most OTC products; Bristol has a history of similar deceptive practices. *See supra* note 3. We agree with the *AHP* court that false claims which consumers are unable to evaluate for themselves, and which encourage the unnecessary use of a

potentially hazardous product, constitute serious violations which help justify the scope of the remedial order. 695 F.2d at 707.

We have considered all of Bristol's claims but find that the Commission quite carefully crafted its remedial order to suit the violations. The Order is broad enough to protect the public while narrow enough to permit compliance without undue burden.

Petition to reverse denied; order enforced.

Appendix: THE COMMISSION'S ORDER

I

IT IS ORDERED that Bristol-Myers Company, its successors and assigns, and its officers, agents, representatives and employees, directly or through any corporation, subisdiary, division or other device, in connection with the advertising, offering for sale, sale or distribution of "Bufferin," "Excedrin," "Excedrin P.M.," or any other nonprescription internal analgesic product, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from:

Making any representation, directly or by implication, that a claim concerning the superior effectiveness or superior freedom from side effects of such product has been established or proven unless such representation has been established by two or more adequate and well-controlled clinical investigations, conducted by independent experts qualified by training and experience to evaluate the comparative effectiveness or comparative freedom from side effects of the drugs involved, on the basis of which it could fairly and responsibly be concluded by such experts (1) that the drug will have the comparative effectiveness or freedom from side effects that it is represented to have, and (2) that such comparative effectiveness or freedom from side effects is demonstrated by methods of statistical analysis, and with levels of confidence, that are generally recognized by such experts. The investigations shall be conducted in accordance with the procedures set forth below.

At least one of the adequate and well-controlled clinical investigations to evaluate the comparative

effectiveness of the drug shall be conducted on any disease or condition referred to, directly or by implication, or, if no specific disease or condition is referred to, then the adequate and well-controlled clinical investigations shall be conducted on at least two conditions or diseases for which the drug is effective. The clinical investigations shall be conducted as follows:

A. The subjects must be selected by a method that:
    1. Provides adequate assurance that they are suitable for the purposes of the investigation, and the diagnostic criteria of the condition to be treated (if any);
    2. Assigns the subjects to the test groups in such a way as to minimize bias;
    3. Assures comparability in test and control groups of pertinent variables, such as age, sex, severity or duration of disease or condition (if any), and use of drugs other than test drugs.

B. The investigations must be conducted double-blind, and methods of double-blinding must be documented. In addition, the investigations shall contain a placebo control to permit comparison of the results of use of the test drugs with an inactive preparation designed to resemble the test drugs as far as possible.

C. The plan or protocol for the investigations and the report of the results shall include the following:
    1. A clear statement of the objective of the investigation;

2. An explanation of the methods of observation and recording of results, including the variables measured, quantitation, assessment of any subject's response and steps taken to minimize bias on the part of the subject and observer;
3. A comparison of the results of treatments or diagnosis with a control in such a fashion as to permit quantitative evaluation. The precise nature of the control must be stated and an explanation given of the methods used to minimize bias on the part of the observers and the analysts of the data;
4. A summary of the methods of analysis and an evaluation of data derived from the study, including any appropriate statistical methods.

D. A test or investigation which is not conducted in accordance with these procedures may be used to establish a claim only if respondent can show that, notwithstanding the failure to satisfy these procedures, the test or investigation would still be generally accepted by the relevant scientific community as sufficient to establish the truth of the claim.

II

IT IS FURTHER ORDERED that respondent Bristol-Myers Company, its successors and assigns, and its officers, agents, representatives and employees, directly or through any corporation, subsidiary, division or other device, in connection with the advertising, offering for sale, sale or distribution of "Bufferin," "Excedrin," or any other

nonprescription internal analgesic, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from making any therapeutic performance or freedom from side effects claim for such product unless respondent possesses a reasonable basis for making that claim. A reasonable basis for such a claim shall consist of competent and reliable scientific evidence supporting that claim. Well-controlled clinical tests conducted in accordance with the criteria set forth in Order Paragraph I shall be deemed to constitute a reasonable basis for a claim.

III

IT IS FURTHER ORDERED that respondent Bristol-Myers Company, its successors and assigns, and its officers, agents, representatives and employees, directly or through any corporation, subsidiary, division or other device, in connection with the advertising, offering for sale, sale or distribution of "Bufferin," "Excedrin," "Excedrin P.M.," or any other nonprescription drug product, in or affecting commerce, as "commerce" and "drug" are defined in the Federal Trade Commission Act, do forthwith cease and desist from:

A. Making any representations, directly or by implication, that such product contains any unusual or special ingredient when such ingredient is commonly used in other nonprescription drug products intended for the same use or uses as the product advertised by respondent.

B. Representing that any group, body, or organization endorses or recommends such product unless at the time such statement or representation is

made, respondent has a reasonable basis for such statement or representation.

IV

IT IS FURTHER ORDERED that respondent Bristol-Myers Company, its successors and assigns, and its officers, agents, representatives and employees, directly or through any corporation, subsidiary, division or other device in connection with the advertising, offering for sale, sale or distribution of "Bufferin," or "Excedrin," or any other nonprescription internal analgesic in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from falsely representing that the analgesic ingredient in an aspirin-containing product is different from aspirin or otherwise misrepresenting the identity of any analgesic ingredient. It shall be a violation of this paragraph to contrast the analgesic ingredient of a product which contains aspirin with the analgesic ingredient of another product if that product also contains aspirin, unless respondent discloses clearly and conspicuously that the analgesic ingredient in its product is aspirin.

V

IT IS FURTHER ORDERED that respondent Ted Bates & Company, Inc., a corporation, its successors and assigns, and its officers, agents, representatives, and employees, directly or through any corporation, subsidiary, division or other device in connection with the advertising, offering for sale, sale or distribution of "Bufferin" or any other nonprescription internal analgesic product, in or affecting commerce, as "commerce" is defined in the

Federal Trade Commission Act, do forthwith cease and desist from:

A. Making any representation, directly or by implication, that such product contains any unusual or special ingredient when such ingredient is commonly used in other nonprescription drug products intended for the same use or uses as the product advertised by respondent.

B. Falsely representing that the analgesic ingredient in an aspirin-containing product is different from aspirin or otherwise misrepresenting the identity of any analgesic ingredient. It shall be a violation of this paragraph to contrast the analgesic ingredient of a product which contains aspirin with the analgesic ingredient of another product if that product also contains aspirin, unless respondent discloses clearly and conspicuously that the analgesic ingredient in its product is aspirin.

C. Representing that any group, body, or organization endorses or recommends such product unless at the time such statement or representation is made respondent has a reasonable basis for such statement or representation.

VI

IT IS FURTHER ORDERED that respondent Young & Rubicam, Inc., a corporation, its successors and assigns, and its officers, agents, representatives, and employees, directly or through any corporation, subsidiary, division, or other device in connection with the advertising, offering for sale, sale, or distribution of "Excedrin," "Excedrin P.M.," or any other nonprescription internal

analgesic product, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from:

A. Making any representation, directly or by implication, that such product contains any unusual or special ingredient when such ingredient is commonly used in other nonprescription drug products intended for the same use or uses as the product advertised by respondent.

B. Falsely representing that the analgesic ingredient in an aspirin-containing product is different from aspirin or otherwise misrepresenting the identity of any analgesic ingredient. It shall be a violation of this paragraph to contrast the analgesic ingredient of a product which contains aspirin with the analgesic ingredient of another product if that product also contains aspirin, unless respondent discloses clearly and conspicuously that the analgesic ingredient in its product is aspirin.

[Parts VII—VIII omitted]

UNITED STATES COURT OF APPEALS
SECOND CIRCUIT

No. 83-4167

At a stated term of the United States Court of Appeals, in and for the Second Circuit, held at the United States Courthouse, in the City of New York, on the 26th day of July one thousand nine hundred and eighty-four.

BRISTOL-MYERS COMPANY,

Petitioner,

v.

FEDERAL TRADE COMMISSION,

Respondent.

A petition for a rehearing having been filed herein by counsel for the petitioner, Bristol-Myers Company,

Upon consideration thereof, it is

Ordered that said petition be and it hereby is DENIED.

/s/ ELAINE B. GOLDSMITH
Elaine B. Goldsmith
Clerk

Final Order

UNITED STATES OF AMERICA
BEFORE FEDERAL TRADE COMMISSION

Docket No. 8917

Commissioners: James C. Miller, III Chairman
David A. Clanton
Michael Pertschuk
Patricia P. Bailey
George W. Douglas

In the Matter of

BRISTOL-MYERS COMPANY,
a corporation,

TED BATES & COMPANY, INC.,
a corporation, and

YOUNG & RUBICAM, INC.,
a corporation.

FINAL ORDER

This matter has been heard by the Commission upon the appeal of counsel for respondents and complaint counsel and upon briefs and oral argument in support of and in opposition to the appeals. The Commission, for the reasons stated in the accompanying Opinion, has granted each appeal in part, and denied each in part. Therefore,

IT IS ORDERED that the initial decision of the administrative law judge be adopted as the Findings of Fact and Conclusions

of Law of the Commission except as is otherwise inconsistent with the attached opinion.

Other Findings of Fact and Conclusions of Law of the Commission are contained in the accompanying Opinion.

IT IS FURTHER ORDERED that the following Order to Cease and Desist be entered:

ORDER

I

IT IS ORDERED that Bristol-Myers Company, its successors and assigns, and its officers, agents, representatives and employees, directly or through any corporation, subsidiary, division or other device, in connection with the advertising, offering for sale, sale or distribution of "Bufferin," "Excedrin," "Excedrin P.M.," or any other nonprescription internal analgesic product, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from:

> Making any representation, directly or by implication, that a claim concerning the superior effectiveness or superior freedom from side effects of such product has been established or proven unless such representation has been established by two or more adequate and well-controlled clinical investigations, conducted by independent experts qualified by training and experience to evaluate the comparative effectiveness or comparative freedom from side effects of the drugs involved, on the basis of which it could fairly and responsibly be concluded by such experts (1) that the drug will have the comparative effectiveness or freedom from side effects that it is represented to have, and (2) that such comparative effectiveness or freedom from side effects is demonstrated by methods of statistical analysis, and with levels of confidence, that are generally recognized by such experts. The investigations shall be conducted in accordance with the procedures set forth below.

At least one of the adequate and well-controlled clinical investigations to evaluate the comparative effectiveness of the drug shall be conducted on any disease or condition referred to, directly or by implication, or, if no specific disease or condition is referred to, then the adequate and well-controlled clinical investigations shall be conducted on at least two conditions or diseases for which the drug is effective. The clinical investigations shall be conducted as follows:

A. The subjects must be selected by a method that:
   1. Provides adequate assurance that they are suitable for the purposes of the investigation, and the diagnostic criteria of the condition to be treated (if any);
   2. Assigns the subjects to the test groups in such a way as to minimize bias; and
   3. Assures comparability in test and control groups of pertinent variables, such as age, sex, severity or duration of disease or condition (if any), and use of drugs other than test drugs.

B. The investigations must be conducted double-blind, and methods of double-blinding must be documented. In addition, the investigations shall contain a placebo control to permit comparison of the results of use of the test drugs with an inactive preparation designed to resemble the test drugs as far as possible.

C. The plan or protocol for the investigations and the report of the results shall include the following:
   1. A clear statement of the objective of the investigation;
   2. An explanation of the methods of observation and recording of results, including the variables measured, quantitation, assessment of any subject's response and steps taken to minimize bias on the part of the subject and observer;

3. A comparison of the results of treatments or diagnosis with a control in such a fashion as to permit quantitative evaluation. The precise nature of the control must be stated and an explanation given of the methods used to minimize bias on the part of the observers and the analysts of the data;
4. A summary of the methods of analysis and an evaluation of data derived from the study, including any appropriate statistical methods.

D. A test or investigation which is not conducted in accordance with these procedures may be used to establish a claim only if respondent can show that, notwithstanding the failure to satisfy these procedures, the test or investigation would still be generally accepted by the relevant scientific community as sufficient to establish the truth of the claim.

II

IT IS FURTHER ORDERED that respondent Bristol-Myers Company, its successors and assigns, and its officers, agents, representatives and employees, directly or through any corporation, subsidiary, division or other device, in connection with the advertising, offering for sale, sale or distribution of "Bufferin," "Excedrin," or any other nonprescription internal analgesic, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from making any therapeutic performance or freedom from side effects claim for such product unless respondent possesses a reasonable basis for making that claim. A reasonable basis for such a claim shall consist of competent and reliable scientific evidence supporting that claim. Well-controlled clinical tests conducted in accordance with the criteria set forth in Order Paragraph I shall be deemed to constitute a reasonable basis for a claim.

III

IT IS FURTHER ORDERED that respondent Bristol-Myers Company, its successors and assigns, and its officers, agents, representatives and employees, directly or through any corporation, subsidiary, division or other device, in connection with the advertising, offering for sale, sale or distribution of "Bufferin," "Excedrin," "Excedrin P.M.," or any other nonprescription drug product, in or affecting commerce, as "commerce" and "drug" are defined in the Federal Trade Commission Act, do forthwith cease and desist from:

A. Making any representations, directly or by implication, that such product contains any unusual or special ingredient when such ingredient is commonly used in other nonprescription drug products intended for the same use or uses as the product advertised by respondent.

B. Representing that any group, body, or organization endorses or recommends such product unless at the time such statement or representation is made, respondent has a reasonable basis for such statement or representation.

IV

IT IS FURTHER ORDERED that respondent Bristol-Myers Company, its successors and assigns, and its officers, agents, representatives and employees, directly or through any corporation, subsidiary, division or other device in connection with the advertising, offering for sale, sale or distribution of "Bufferin," or "Excedrin," or any other nonprescription internal analgesic in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from falsely representing that the analgesic ingredient in an aspirin-containing product is different from aspirin or otherwise misrepresenting the identity of any analgesic ingredient. It shall be a violation of this paragraph to contrast the analgesic ingredient of a product which contains aspirin with the analgesic ingredient of another product if that product also contains aspirin, unless respondent discloses clearly and con-

spicuously that the analgesic ingredient in its product is aspirin.

V

IT IS FURTHER ORDERED that respondent Ted Bates & Company, Inc., a corporation, its successors and assigns, and its officers, agents, representatives, and employees, directly or through any corporation, subsidiary, division or other device in connection with the advertising, offering for sale, sale or distribution of "Bufferin" or any other nonprescription internal analgesic product, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from:

A. Making any representation, directly or by implication, that such product contains any unusual or special ingredient when such ingredient is commonly used in other nonprescription drug products intended for the same use or uses as the product advertised by respondent.

B. Falsely representing that the analgesic ingredient in an aspirin-containing product is different from aspirin or otherwise misrepresenting the identity of any analgesic ingredient. It shall be a violation of this paragraph to contrast the analgesic ingredient of a product which contains aspirin with the analgesic ingredient of another product if that product also contains aspirin, unless respondent discloses clearly and conspicuously that the analgesic ingredient in its product is aspirin.

C. Representing that any group, body, or organization endorses or recommends such product unless at the time such statement or representation is made respondent has a reasonable basis for such statement or representation.

VI

IT IS FURTHER ORDERED that respondent Young & Rubicam, Inc., a corporation, its successors and assigns, and its officers, agents, representatives, and employees, directly or

through any corporation, subsidiary, division, or other device in connection with the advertising, offering for sale, sale, or distribution of "Excedrin," "Excedrin P.M.," or any other nonprescription internal analgesic product, in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from:

A. Making any representation, directly or by implication, that such product contains any unusual or special ingredient when such ingredient is commonly used in other nonprescription drug products intended for the same use or uses as the product advertised by respondent.

B. Falsely representing that the analgesic ingredient in an aspirin-containing product is different from aspirin or otherwise misrepresenting the identity of any analgesic ingredient. It shall be a violation of this paragraph to contrast the analgesic ingredient of a product which contains aspirin with the analgesic ingredient of another product if that product also contains aspirin, unless respondent discloses clearly and conspicuously that the analgesic ingredient in its product is aspirin.

VII

IT IS FURTHER ORDERED that respondents Bristol-Myers Company, Ted Bates & Company, Inc., and Young & Rubicam, Inc., shall notify the Commission at least thirty (30) days prior to any proposed change in their respective corporate respondent such as a dissolution, assignment or sale resulting in the emergence of a successor corporation, the creation or dissolution of subsidiaries or any other change in their respective corporation which may affect compliance obligations under this Order.

VIII

IT IS FURTHER ORDERED that the respondents herein shall within sixty (60) days after service of this Order upon them, and at such other times as the Commission may require, file

with the Commission a written report setting forth in detail the manner and form in which they have complied or intend to comply with this Order.

Paragraphs Seven A.3, Seven A.4, Seven B.3, Seven B.4, Seven B.5, Seven B.8, Seven B.9, Seven B.10, Nine, Ten, Eleven, Twelve C, Fourteen, Fifteen, Sixteen, Twenty-Three, and Twenty-Four of the Complaint are hereby dismissed.

By the Commission.

/s/ EMILY H. ROCK
Emily H. Rock
Secretary

ISSUED: July 5, 1983

Attachments: Concurring Statement by Chairman Miller
Separate Statement Concurring in Part and Dissenting in Part by Commissioner Pertschuk
Separate Statement Concurring in Part and Dissenting in Part by Commissioner Bailey
Concurring Statement by Commissioner Douglas

Opinion of the Commission

UNITED STATES OF AMERICA
BEFORE FEDERAL TRADE COMMISSION

Docket No. 8917

Commissioners: James C. Miller, III Chairman
David A. Clanton
Michael Pertschuk
Patricia P. Bailey
George W. Douglas

In the Matter of

BRISTOL-MYERS COMPANY,
a corporation,

TED BATES & COMPANY, INC.,
a corporation, and

YOUNG & RUBICAM, INC.,
a corporation.

OPINION OF THE COMMISSION

By Clanton, Commissioner:

I INTRODUCTION AND HISTORY OF THE CASE

Announcer: Excedrin headache #94102: The Parking Attendant.

Man 1: This is a red sedan.

Man 2: Yes it is. Take your red sedan and move it out on the street, or we'll push it out . . . .

Thus begins an ad for Excedrin, an over-the-counter (non-prescription or "OTC") aspirin-based analgesic (pain reliever) produced by the Bristol-Myers Company ("Bristol-Myers"). From 1971 to 1973, consumers spent an average of $85 million annually to purchase Excedrin, Bufferin, and Excedrin P.M., all of which are manufactured by Bristol-Myers. During that same time, Bristol-Myers spent approximately $20 million each year to promote the sale of these three products with television, radio, and print advertisements. That some of these ads were very clever (such as the "Excedrin headache #____" campaign mentioned above) or very effective (as demonstrated by Bristol-Myers' sales) is unquestioned. What is at issue in this proceeding is whether the claims made for these products violate the law.

The issues involved here are very similar to those involved in *American Home Products Co.*, 98 F.T.C. 136 (1981), *aff'd*, 695 F.2d 681 (3d Cir. 1982), and in *Sterling Drug, Inc.*, Docket No. 8919 (also announced today). In each of these three companion cases, we are required to determine (a) what claims were made by various analgesic advertisements, (b) what level of evidence should be required to substantiate those claims, and (c) whether the evidence possessed by the advertisers measures up to that required level. Each case involved a number of advertising claims, made in a large number of separate advertisements.

In brief, in this case (as in the others), we find that respondent made some claims for which it lacked a reasonable basis, in violation of the doctrine of *Pfizer, Inc.*, 81 F.T.C. 23 (1972). We also find that in a large number of advertisements respondent represented that claims had been scientifically established even though respondent's evidence did not bear out this contention. However, we decline to follow our prior decision in *American Home Products*, insofar as it found consumers believe every comparative performance claim has been scientifically established (the "substantial question" theory). Thus, in this case and in *Sterling Drug*, we hold the advertiser to the level of evidence required to convince the relevant scientific community of the claim's truthfulness only when the advertisement espressly or implicitly represents that the claim's truth has been scientifically established.

The Commission issued the complaint against Bristol-Myers and against Ted Bates & Company, Inc., and Young & Rubicam, Inc., Bristol-Myers' advertising agencies, on February 23, 1973.[1] The complaint charged that respondents' advertising violated Sections 5 and 12 of the Federal Trade Commission Act (15 U.S.C. §§45, 52) by making advertising claims regarding Bufferin's efficacy, freedom from side effects, ability to relieve tension, and ingredients and regarding Excedrin and Excedrin P.M.'s efficacy, ability to relieve tension and ingredients. Ted Bates and Company, Inc. was charged with responsibility for all ads relating to Bufferin and Young & Rubicam, Inc. was charged with responsibility for the claims relating to Excedrin and Excedrin P.M.

This case was assigned for hearing to Administrative Law Judge Montgomery K. Hyun, who rendered an initial decision finding against respondent Bristol-Myers on all charges except those relating to claims that Bufferin is twice as strong as aspirin (Comp. ¶ 7(A)(3), 9(A)(3), and part of 14(A)) and that Excedrin P.M. is an effective sedative (Comp. ¶ 12(C)). With respect to the advertising agencies, Judge Hyun found that they had adequate substantiation for all comparative safety and efficacy claims but found them liable for failing to disclose the presence of aspirin in the products.

This matter is now before the Commission on the appeal of all three respondents and complaint counsel. Respondent Bristol-Myers' principal contentions on appeal are: (1) the ALJ erred in interpreting the meanings of the challenged ads; (2) the ALJ erred in finding that Bristol-Myers lacked substantiation for the claims made in its advertisements; (3) there is no legal support for the clinical testing standard which the ALJ's order requires as substantiation for comparative claims; and (4) the ALJ's order is overbroad and violates Bristol-Myers' constitu-

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1 On the same date, the Commission issued a complaint against American Home Products Corporation regarding its advertising of Anacin and Arthritis Pain Formula and a complaint against Sterling Drug, Inc., regarding its advertising of Bayer Aspirin, Bayer Children's Aspirin, Cope, Vanquish, and Midol.

tional rights. Both advertising agencies appeal on the grounds that they acted reasonably in relying on Bristol-Myers' substantiation and the ALJ erred in entering any order against them. Complaint counsel support the ALJ's order and findings in most respects but raise the following issues on appeal: (1) corrective advertising should have been ordered; and (2) the ALJ erred by not finding the ad agencies liable for establishment claims.

In our discussion below, we will review each claim in turn, first determining whether the claim was made by the advertisements and then describing the standard by which the respondent's substantiation is to be judged. At the end, we discuss the liability of the two advertising agencies.[2]

II. Comparative Efficacy and Side Effects Claims

A. Legal Standards for Interpreting Claims

Paragraphs 7 through 11 of the complaint contain two sets of allegations regarding respondent Bristol-Myers' comparative performance claims for Bufferin, Excedrin, and Excedrin P.M. and we deal with these claims in this section. In Part B below, we consider the representations made by respondent's advertisements. First, however, we consider the manner in which the meaning of advertisements is interpreted under Section 5 of the F.T.C. Act.

Interpreting advertising claims is not a mystical process; it involves the exercise of common sense and good judgment. *F.T.C.* v. *Colgate-Palmolive Co.*, 380 U.S. 374, 385 (1965); *Porter & Dietsch*, 90 F.T.C. 770, 862 n.3, *aff'd as modified*,

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2 The following abbreviations are used in this opinion:

F.	— Initial Decision, Finding No.
I.D.	— Initial Decision
CX	— Complaint Counsel's Exhibit No.
RX	— Respondents' Exhibit No.
Tr.	— Transcript of Testimony, Page No.
RAB	— Bristol-Myers Appeal Brief
C.A.B.	— Complaint Counsel's Appeal Brief
C.R.A.B.	— Complaint Counsel's Revised Answering Brief

605 F.2d 294 (7th Cir. 1979). It is well settled that the Commission can determine the meaning of an advertisement without necessarily resorting to assessments of consumer perception or other expert testimony. *American Home Products* v. *F.T.C.*, 695 F.2d at 687, and cases cited at n. 10; *The Kroger Company*, 98 F.T.C. 639, 728 (1981). However, when extrinsic evidence on the meaning of an ad has been introduced, that evidence must be considered by the Commission in reaching its conclusion. *Cinderella Career and Finishing Schools, Inc.* v. *F.T.C.*, 425 F.2d 583, 588 (D.C. Cir. 1970); *The Kroger Company*, 98 F.T.C. at 729 n. 11. While that evidence will not necessarily supplant the Commission's common sense judgment, it will assist us in reaching a sound decision. *Firestone Tire and Rubber Co.*, 81 F.T.C. 398, 454 (1971), *aff'd* 481 F.2d 246 (6th Cir. 1973), *cert. denied*, 414 U.S. 1112 (1973); *Crown Central Petroleum Corp.*, 84 F.T.C. 1493, 1540 (1974). There also may be instances where claims cannot be inferred from a facial examination of the advertisements and resort to extrinsic evidence is necessary. *See e.g., Leonard F. Porter, Inc.*, 88 F.T.C. 546, 626 (1976).

When the Commission interprets an ad, it must consider the net impression that the ad makes on consumers. *American Home Products* v. *F.T.C.*, 695 F.2d at 688; *National Bakers Services, Inc.* v. *F.T.C.*, 329 F.2d 365 (7th Cir. 1964). Thus, an ad may violate the law if an implied representation which it conveys is not properly substantiated, even though the statements in the advertisement taken literally are true. *Carter Products, Inc.* v. *F.T.C.*, 323 F.2d 523, 528 (5th Cir. 1963). But the Commission may not inject novel meanings into ads and then strike them down as unsupported; ads must be judged by the impression they make on reasonable members of the public. *Ward Laboratories, Inc.* v. *F.T.C.*, 276 F.2d 952, 954 (2nd Cir. 1960), *cert. denied*, 364 U.S. 827 (1960); *International Parts Corporation* v. *F.T.C.*, 133 F.2d 883 (7th Cir. 1943). *Heinz W. Kirchner*, 63 F.T.C. 1282, 1290 (1963), *aff'd* 337 F.2d 751 (9th Cir. 1964). If an ad conveys more than one meaning to reasonable consumers and one of those meanings is false, that ad may be condemned. *National Commission on*

Egg Nutrition v. *F.T.C.*, 570 F.2d 157, 161 n.4 (7th Cir. 1977), *cert. denied*, 439 U.S. 821 (1978).

Finally, the challenged claims must be material to the purchase decision; in other words, the claims must be of the type that consumers are likely to rely upon in deciding whether to purchase a particular good or service. *F.T.C.* v. *Colgate-Palmolive Co.*, 380 U.S. at 386.[3] (Respondent does not dispute the materiality of the claims it is charged with making. However, it does dispute the materiality of its failure to disclose the presence of aspirin in ads for Bufferin and Excedrin.) With this background, we now turn to Bristol-Myers' ads.

B. Representations of Comparative Efficacy and Freedom from Side Effects in Bristol-Myers' Ads

Complaint paragraphs 7-11 charge respondent with making numerous claims of superior efficacy and freedom from side effects for Bufferin, Excedrin, and Excedrin P.M. Paragraphs 7 and 8 charge that the ads represented that the claims had been established. Paragraphs 9-11 allege that where there was no representation of establishment, respondents failed to disclose the existence of a substantial question regarding the claims' validity.

In the Initial Decision, Judge Hyun found that respondent had made 14 of the 15 challenged claims of superior performance or freedom from side effects and that it had represented that all 14 of these claims had been established.[4] We agree with respect to ten of the performance claims and seven of the establishment claims.[5] We disagree, however, with Judge

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3 Under Section 15 of the F.T.C. Act, materiality is an essential element of a false advertising charge involving drugs. 15 U.S.C. § 55(a).

4 F. 233-363. Judge Hyun found that respondent did not make the claims alleged by complaint paragraphs 7(A)(3) and 9(A)(3) (that a recommended dose of Bufferin relieves twice as much pain as a recommended dose of aspirin will relieve and that that fact has been established) (I.D. pp. 209-210). Complaint counsel have not appealed this and we see no reason to reverse the ALJ's decision on this point.

5 We find that some of the ads used by the ALJ as examples to support claims which were made do not support those claims. Although we

Hyun's finding that every ad that makes a comparative claim also represents that the claim has been established.[6]

In analyzing the claims involved in this case, it will help to keep in mind three different categories of claims. The first consists of "puffing" claims, which are not capable of measurement or which consumers would not take seriously—for example, an advertisement touting a foreign sports car as "the sexiest European." These claims do not require any substantiation. *See Pfizer, Inc.*, 81 F.T.C. at 64 (1972).

The second and third categories consist of claims which, under the *Pfizer* doctrine, do require some level of substantiation. If an advertisement represents that a particular claim has been scientifically established—what we will refer to here as an "establishment claim"—then, under *Pfizer*, the advertiser must possess the level of proof claimed in the ad. When an advertiser makes an establishment claim, it must possess evidence sufficient to satisfy the relevant scientific community of the claim's truth. If an ad does not assert that a claim has been established, then the advertiser is only required to have a "reasonable basis" for believing that the claim is true. As we discussed in *Pfizer*, the evidence required to constitute a "reasonable basis" in such a case will depend on various factors including the importance of the claim being made, the consequences to consumers if the claim is false, and the ease with which more reliable evidence could be acquired.

A key issue, then, is whether each advertisement represents that a given claim has been scientifically established. Although an establishment claim may be made by such words and phrases as "established," "here's proof," and "medically proven," *see American Home Products*, 98 F.T.C. at 374; *Standard Oil Co. of California*, 84 F.T.C. 1401, 1472 (1974), *modified on other grounds*, 577 F.2d 653 (9th Cir. 1978), it

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find a smaller number of violative ads than did the ALJ, there is certainly an adequate number to support the order provisions which we enter today. See Fedders Corp., 85 F.T.C. 38, 71-72 (1975).

6 F. 266, 357; I.D. p. 213.

may also be made through the use of visual aids (such as scientific texts or white-coated technicians) which clearly suggest that the claim is based upon a foundation of scientific evidence.[7] *See American Home Products*, 98 F.T.C. at 375. Furthermore, the representation of establishment need not be made explicitly in an ad but may be implicit. *American Home Products* v. *F.T.C.*, 695 F.2d at 689-690.

1. *Claims that Bufferin relieves pain faster than aspirin and that it relieves pain twice as fast as aspirin.*[8]

Although Bristol-Myers argues there was no showing the ads in question made this claim, (R.A.B. 47-48), we agree with the ALJ that numerous ads made the representation that Bufferin was faster acting. Furthermore, we believe that consumers would reasonably conclude that the claim of superior speed had been established.

First, Bristol-Myers has admitted its ads represented Bufferin relieves pain faster than aspirin.[9] Of course, this representation is also made by ads which represent that Bufferin relieves pain twice as fast as aspirin because this statement simply is a more extreme version of the claim. For example, CX 3 states:

> In the first important 30 minutes Bufferin delivers twice as much pure pain reliever as the best known aspirin. Twice as much.[10]

Although read literally, this ad states twice as much Bufferin is going to work, consumers could reasonably have understood this is to mean Bufferin relieves pain twice as fast as aspirin.

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7 This is not to say that every reference to a test necessarily gives rise to an establishment claim. The key, of course, is the overall impression created by the ad. Cf. Pfizer, 81 F.T.C. at 59.

8 Complaint paragraphs 7(A)(1), (2) and 9(A)(1), (2).

9 Answer of Bristol-Myers, paragraph 7.

10 Similar language was used in CX 2, 4, 7, 10, 12, 13, 15, 61, 63, 64, 67.

And, in fact, this is confirmed by a copy test in the record which measured viewer reactions to an ad containing this language (CX 301 M). The same representation was made more directly by advertisements which state Bufferin goes to work in half the time. For example, CX 22 states:

> Bufferin can cut the waiting time in half. Half the time. That's Bufferin time. Because in the first critical minutes, Bufferin acts twice as fast as simple aspirin to speed more of its active pain reliever to your headache. Bufferin goes to work in half the time.[11]

Once again, consumers could reasonably infer from this that Bufferin relieves pain faster and this is confirmed by a copy test in the record. *See* CX 245.

We are unable to agree with the ALJ that every ad making a comparative performance claim also represented that superiority had been established. However, we find that some of respondent's ads do make that claim. For example, CX 61 states:

> Scientific tests show that in the first critical moments Bufferin delivers twice as much pain reliever as simple aspirin.[12]

As another example, CX 34 states:

> Tests show Bufferin's high-speed formula rushes its pain reliever to your headache twice as fast as aspirin.

Other ads represent that it has been established that Bufferin relieves pain faster (not necessarily twice as fast) as aspirin. For example, CX 91 states:

> Bufferin laboratory tests show most of its pain reliever gets in the bloodstream 10 minutes sooner than plain aspirin.[13]

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11 Similar language was used in CX 1, 23-39.

12 Similar language appears in CX 63, 64.

13 Similar language appears in CX 761Z018.

None of Bristol-Myers' ads actually uses the word "established."[14] However, this is immaterial because the ads create the impression that the claims have been established. (*See supra* p.6.) *American Home Products* v. *F.T.C.*, 695 F.2d at 690. The impression conveyed by these ads comes not only from the words but also from visual images which have been used. For example, in CX 61, 63, and 64, a computer typewriter prints out a column made up of the words "Bufferin" and "aspirin" on graph paper at the same time as the announcer speaks about scientific tests. The column representing Bufferin prints out twice as fast and twice as high as the column for aspirin. It appears to be printing the results of the scientific test in a graphic form showing Bufferin to be superior. Consumers could reasonably conclude that proof acceptable to scientists underlies the claim made in the advertisement.

We disagree, however, with the ALJ regarding some of respondent's ads. Although the computer typewriter enhances the implication of establishment in the three ads discussed above, we do not think that it alone can create the impression of scientific support for the claim.[15] Similarly, we do not think that glass models of people with Bufferin and aspirin tablets crumbling in their stomachs and reforming in their heads indicates that Bufferin's superior speed has been scientifically established.[16] Although these props are effective in conveying the claim of Bufferin's superior speed, they do not add an aura of scientific establishment to the claim.[17] Thus, we find that the ads which contain only these props do not make a representation of establishment.

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14 The word "established" was used in two magazine advertisements for Bufferin during the 1950s. See CX 100, 101.

15 CX 2, 4, 7, 67; see F. 270.

16 CX 68-77; see F. 270.

17 This is not to say that props alone can never create a representation of establishment. Indeed, a depiction of test apparatus or the use of an announcer in a white technician's coat, in the right context, might constitute a representation of scientific establishment.

2. *Claims that Bufferin will not upset a person's stomach and that it does so less frequently than aspirin.*[18]

Respondent has admitted its ads represent Bufferin will not upset a person's stomach as often as aspirin,[19] and our examination of the ads shows that this message is plainly conveyed.[20] Respondent's ads also represented that Bufferin will not upset a person's stomach. This message is contained in CX 2, "Bufferin doesn't upset my stomach the way plain aspirin sometimes did."[21] Other ads use the following phrases, "without the stomach upset plain aspirin can cause," and "without fear of stomach distress."[22] A copy test in the record also confirms that consumers received the "no stomach upset" message from the ads. (CX 301N)

The ALJ found that three of the challenged advertisements made establishment claims that Bufferin will not upset a person's stomach (CX 61, 63, 64). We are unable to agree with this conclusion. These ads deal primarily with Bufferin's ability to provide pain relief and contain language similar to the following:

> Scientific tests show that in the first critical minutes, Bufferin delivers twice as much pain reliever as simple aspirin. Bufferin relieves arthritis, minor pain, and stiffness for hours. So hands and fingers regain flexibility. . . . And Bufferin can prevent the stomach upset aspirin often causes. (CX 61)

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18 Complaint paragraphs 7(A)(4), 7(A)(5), 9(A)(4), and 9(A)(5).

19 Answer of Bristol-Myers Company paragraph 7.

20 For example, CX 11 states, "without the stomach upset plain aspirin can cause." This ad, and others like it, represent both that Bufferin upsets the stomach less than aspirin and also that Bufferin does not upset the stomach. Other ads which represent that Bufferin upsets the stomach less than aspirin are, e.g. CX 2-7, 17, 19, 41, 43-46.

21 See also CX 3-7, 40, 41, 43, 66.

22 See CX 11, 17, 19, 44-46, 96.

As explained above, we agree that this ad represents that Bufferin's superior speed has been established. The ALJ apparently concluded that the reference to scientific testing imbued *all* subsequent claims with the aura of medical-scientific authority. We are not convinced this is the impression consumers would receive. Although complaint counsel's expert witness stated consumers would infer that scientific tests supported the series of claims that followed, including the gentleness claim (Tr. 7019-7020), we are unable to reach that conclusion without further evidence of consumer beliefs. Indeed, the reference to stomach upset is preceded by a pause which separates it from claims represented to be supported by scientific proof. The pause signals a change of subject. We, therefore, cannot find that respondent represented it has been established Bufferin will not upset one's stomach.

However, respondent clearly represented it had been established that Bufferin will upset the stomach less frequently than aspirin. CX 109 states, "It has been clinically observed that Bufferin was gentler to the stomach than plain aspirin." Although, once again, the word "establishment" is not actually used, we believe consumers receive an impression of scientific proof from this ad.

3. *Claims that Excedrin relieves twice as much pain as aspirin and more pain than any other over-the-counter analgesic.*[23]

The ALJ found respondent had made both these claims[24] and we agree. In some advertisements Excedrin is represented as able to relieve more pain than aspirin. For example, CX 115 states, "Tablet for tablet, Excedrin is 50% stronger than aspirin for the relief of headache pain."[25] Although this ad actually says that Excedrin is stronger for the relief of pain than aspirin, consumers could reasonably interpret this ad to

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23 Complaint paragraphs 7(b)(1), (2) and 9(B)(1), (2).

24 F. 274-277, 289-292.

25 Some other examples of this claim are CX 116, 162, 163.

say that Excedrin relieves more pain. In addition, this claim is made by those ads which represent that Excedrin relieves twice as much pain as aspirin. CX 153 says:

> It would take more than twice as many aspirin tablets to give the same pain relief as two Excedrin. Not three aspirin. Not even four. But more than double the recommended dosage to give the same pain relief as two Excedrin.[26]

Again, read literally this ad does not say that Excedrin relieves twice as much pain. Nevertheless, that claim is a natural implication of the ad's explicit assertions regarding the relative potency of Excedrin and aspirin.

None of respondent's ads compares Excedrin to all other over-the-counter analgesics. However, numerous ads make a comparison to other "leading tablets." For example, CX 169 states, "Excedrin has more pain relievers, more total strength than any other leading tablet."[27] Consumers could reasonably infer that a tablet which is a leading tablet has achieved that status, at least in part, through its ability to relieve pain. Since Excedrin is represented as being better than its leading competitors, consumers could assume that Excedrin is the best of all. *See American Home Products*, 98 F.T.C. at 372.

The ALJ found that the challenged ads made establishment claims that Excedrin relieves more pain than either aspirin or any other OTC analgesic and that Excedrin relieves twice as much pain as aspirin. We find that respondent did make the claim alleged with respect to Excedrin's superiority over aspirin. For example, CX 203 states:

> What's better than aspirin? New clinical evidence says Excedrin. In a major hospital study, two Excedrin worked better in relieving pain than twice as many aspirin tablets.

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26 Some other examples of this claim are CX 154-161, 170, 171, 202-204.

27 Other examples of this claim are CX 122, 123, 126-128, 134, 136, 137, 174, 178.

Indeed, a series of television commercials focuses totally on the results of the "major hospital study."[28] These ads are set in Atlantic City and start:

> This is where it all happened. At a medical convention right here in Atlantic City. Here doctors heard new clinical evidence that there is a difference in how pain relievers perform. . . . (CX 155)

Another ad in the series discusses the history of such medical tests (CX 176) and still others discuss some of the details of the study (e.g. CX 167, 182). Finally, the ads stress that consumers should rely on the results of this study, "With that kind of medical evidence, isn't it time you tried Excedrin?" (CX 173).

However, we disagree with the ALJ's finding that Bristol-Myers made an establishment claim that Excedrin relieves more pain than *all* other OTC analgesics. The ALJ cites 11 ads which he believes make this representation (F. 321). However, upon examining these ads, we cannot conclude that they represent that Excedrin relieves more pain. All 11 ads are similar. All contain a graphic representation of Excedrin's formula and language similar to the following:

> The modern Excedrin formula gives you quick relief, long-lasting relief, a tension-reliever to relax you, an antidepressant to help restore your spirits. Four ingredients . . . not just one or two. That's Excedrin . . . the Extra-Strength pain reliever. (CX 132)[29]

Although we believe that this ad does compare Excedrin to other products, the comparison is with respect to overall efficacy, not just pain relief (see infra pp. 15-16). Furthermore, the ad does not represent that Excedrin is the only extra-strength OTC analgesic available. Finally two copy tests in the record (CX 289, 290) relate to ads containing this language and

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28 CX 153-161, 164-167, 170, 171, 173, 176, 182, 184, 185, 202-204.

29 The other ten ads are CX 115, 116, 124, 125, 133, 138, 139, 141, 142, 144.

both indicate that only a small number of viewers received the impression that Excedrin was the strongest pain reliever.[30]

4. *Claims that Excedrin relieves pain faster and for a longer period of time than aspirin or any other OTC analgesic.*[31]

We are unable to agree with the ALJ that respondent made either of these representations in its advertisements. The ALJ found that the faster-acting claim was made by two types of ads. The first type states that Excedrin "has a special type of ingredient for quick relief."[32] There is, however, no comparison in the ad between Excedrin's speed and the speed of any other product.[33] We are unwilling to read such an implication into those ads without some strong evidence that consumers receive the "faster acting" message from an ad which merely says "fast acting."[34] The ALJ also found that any ad that claimed that Exedrin was stronger made an implicit representation that Excedrin was faster acting. He based this conclusion upon the expert testimony of Dr. Ivan Ross. Dr. Ross' com-

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30 The record contains numerous surveys ("copy tests") which measure viewer reactions to ads. Because of the way in which these studies are conducted (F. 185-215) participants tend to focus only on the primary idea of the ad being tested and the results are not statistically projectable to the population at large. While this does make the copy tests less useful for our purposes, they are of help to us in confirming whether our interpretation of certain claims is reasonable. See American Home Products v. F.T.C., 695 F.2d at 687.

31 Complaint paragraphs 7(B)(3), (4) and 9(B)(3), (4).

32 E.g., CX 115, 116, 124, 125, 137-139, 141, 142, 144.

33 Some of the ads do make very specific fast-acting claims. For example, CX 115 features an endorsement of a user whose headache disappeared in ten minutes. Nonetheless, there is no comparison with other products.

34 The record contains two tests of consumer reactions to the fast acting claim. In one test 3% of the viewers inferred a faster acting claim (CX 290). In the other, 15% drew the inference (CX 289). We do not find this to be strong enough evidence to conclude that a significant number of reasonable consumers would draw the inference from the ad.

ments were conclusory in nature and we do not find them persuasive based upon consumer response to the ads.

The ALJ found noncomparative ads such as CX 125 claimed Excedrin provided longer lasting relief. That ad states, "The modern Excedrin formula gives you . . . long lasting relief . . . ." Although the Initial Decision refers to tests of consumer reactions to advertisements (F. 294), these tests do not show that any significant number of consumers derived a "longer lasting pain relief" message from the ads. Once again, without such evidence, we are unable to reach the conclusion drawn by the ALJ. The ALJ concluded that the "longer lasting" message was conveyed by any ad that represented Excedrin as being either stronger or more effective. The only evidence in the record to support this proposition is the testimony of complaint counsel's expert Dr. Ross (Tr. 7058-9, 7066, CX 819). As we stated above, we do not find this evidence adequately convincing to permit us to conclude that consumers would receive the impressions from the ads.

5. *Claims that Excedrin reduces fever more effectively than aspirin.*[35]

We agree with the ALJ that this claim was made in three ads, each of which indicates that Excedrin has more "fever reducers." (CX 162, 163, 186) We believe that reasonable consumers could infer that the presence of more "fever reducers" in the product implies that the product is more effective at reducing fever. None of these ads claims that Excedrin's superior fever-reducing capacity has been established and the ALJ concedes as much (F. 288). Since, as we indicated above (p. 8), we are unable to conclude that every claim of comparative superiority implies that the superiority has been established, we find that respondent did not make the challenged establishment claims.

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35 Complaint paragraphs 7(B)(5) and 9(B)(5).

6. *Claims that Excedrin is a more effective pain reliever than aspirin or any other OTC analgesic and that it is more effective because it has four ingredients.*[36]

Respondent has admitted representing that Excedrin is a more effective pain reliever than aspirin.[37] The ALJ found that respondent had represented not only that Excedrin was more effective than aspirin, but also that it was more effective than any other OTC analgesic. We agree. Statements such as "Excedrin is made stronger against pain and stronger against its tension than any other leading headache tablet," (CX 122) and "Excedrin has more pain relievers, more fever reducers, more total strength than any other leading tablet," (CX 186) proclaim that Excedrin is a more effective pain reliever than any other OTC analgesic.[38] As explained above, (*supra* p. 11), a comparison between Excedrin and "any other leading tablet" could be viewed by consumers as a comparison with all other analgesics. Furthermore, we find that ads which promote Excedrin's superior strength are, in fact, representing that Excedrin is a superior pain reliever. The fact that consumers receive this impression is supported by copy test results in the record. (CX 288)

We also find that respondents represented that Excedrin is a more effective pain reliever because it has four ingredients. (Of course, each ad which makes this claim also makes a claim of superior efficacy as discussed in the preceding paragraph, since the four-ingredient claim merely adds an explanation of the reason for the superiority.) However, we find that respondent offered this reason only in representing that Excedrin was only

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36 Complaint paragraphs 7(B)(6), (7) and 9(B)(6), (7).

37 Answer of Bristol-Myers, para. 7. Examples of this claim are CX 116, 153-167, 176, 179-182, 188-191, 199-208, 752-759. A claim of superior effectiveness relative to aspirin was also made by any ad which stated that Excedrin relieved more pain or twice as much pain as aspirin, as discussed above at pp. 10-12.

38 Examples of similar representations are contained in CX 123, 126-128, 136, 137, 169, 172, 174, 178, 186, 737, 738, 740, 741.

more effective than aspirin, and not in representing that it was more effective than all other OTC analgesics. For example, CX 115 states:

> Look: this is the formula for aspirin. The heavily-advertised product that talks of a new stronger formula merely adds caffeine to plain aspirin. But Excedrin has the strength of four medically-endorsed ingredients. You get quick relief . . . long-lasting relief, . . . a tension reliever to relax you, . . . an anti-depressant to restore your spirits.[39]

As these lines are being spoken, there is a video depiction of benzene rings showing, first, aspirin's formula, then the "heavily advertised product's" formula, and then Excedrin's formula with four ingredients. The message conveyed by this ad is that Excedrin is stronger, based on the reference to the "strength of four medically-endorsed ingredients," and enhanced by the video comparison which shows Excedrin with more benzene rings than either of the other two products.

Our interpretation of these ads is consistent with our interpretation of similar ads in *American Home Products*. There we held that an ad (CX 15) which showed Anacin's formula made a representation of superior efficacy because the ad showed Anacin as having more of the pain relieving ingredient. 98 F.T.C. at 375. We find that in ads like CX 115 respondent depicts Excedrin as having four ingredients to provide strength. The ad thereby represents that Excedrin is a more effective pain reliever than aspirin. However, CX 115 specifically mentions and depicts the formulas of the two analgesics to which Excedrin is being compared and in the context of this ad, the comparison is clearly limited to those two. Consumers would not infer that Excedrin is being compared to all OTC analgesics.

However, we are unable to agree with the ALJ that this same message was conveyed by every ad which mentioned Excedrin's

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39 Other similar ads are CX 116, 200, 201.

four ingredients. For example, CX 125 closes with a graphic depiction of Excedrin's formula and the following language:

> The modern Excedrin formula gives you quick relief, long lasting relief, a tension reliever to relax you, an anti-depressant to help restore your spirits. Four ingredients, not just one or two.[40]

Although this ad does imply that Excedrin is better, the message conveyed by the language is that it is better because it performs more functions—not only does it relieve pain, but it also relieves tension and contains an anti-depressant. Only two of the ingredients are devoted to pain relief; one provides quick pain relief and the other provides long-lasting relief. Thus, unlike CX 115, this ad does not say that the four ingredients make it a better pain reliever; it says only that Excedrin is better because it has four ingredients which enable it to cure a variety of problems that cannot be cured by an analgesic containing only one or two ingredients.

We also find that CX 115 makes an establishment claim that Excedrin is a more effective pain reliever than aspirin because it has four ingredients. This representation is conveyed by the description of the ingredients as "medically endorsed" ingredients and by the use of the graphic display of Excedrin's chemical formula. The use of the language and the image imbue the ads with an aura of scientific support which we believe reasonable consumers would perceive. These two ads also necessarily represent that it has been established that Excedrin is a more effective pain reliever than aspirin. There are other ads which make this same representation. For example, CX 155 states that at a medical convention doctors were presented with clinical evidence which showed that Excedrin was a more effective pain reliever. The use of the words "clinical" and "evidence" and the reference to a "major hospital study" imply that the claim in the advertisement is backed by a level of substantiation which would satisfy doc-

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40 Similar language is used in CX 124, 132, 133, 138, 139, 141, 142, 144.

tors. Thus, consumers would infer from the ad that Excedrin's superior efficacy over aspirin has been established.[41] However, we find no ads which represent that it has been established that Excedrin is a more effective pain reliever than any other OTC analgesic.

7. *Claims that Excedrin P.M. will relieve more pain than a recommended dose of aspirin and that it is a more effective pain reliever than aspirin because it has three analgesic ingredients.*[42]

We agree with the ALJ that rspondent represented that Excedrin P.M. will relieve more pain than aspirin. For example, CX 236 states, "Well, let me tell you about Excedrin P.M. It has more pain relievers than simple aspirin. . . ."[43] As we found in connection with representations regarding Excedrin (*supra* p. 11), consumers could reasonably infer that a product which contains more pain relievers than aspirin would relieve more pain than aspirin. However, we find that some of the ads cited by the ALJ as representing Excedrin P.M.'s ability to relieve more pain contain no comparison, either direct or implied, to aspirin. We find the same to be true of all ads cited by the ALJ as representing that Excedrin P.M. is a superior pain reliever because it contains three analgesic ingredients. Although these ads mention the ingredients in Excedrin P.M., none mentions aspirin. For example, CX 233 compares Excedrin P.M. only with Excedrin and CX 244 mentions no other product. Our conclusion is supported by copy test results in the record which show that consumers did not infer a claim of comparative efficacy from ads which did not mention other products. (*See* CX 263.) Thus we find that respondent did not represent that Excedrin P.M. is a more effective pain reliever than aspirin because it has three analgesic ingredients.

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41 Numerous ads make the same establishment claim. Among them are CX 153, 154, 156-161, 164-167, 170, 171, 202-206.

42 Complaint paragraphs 7 (B) (8), (10) and 9 (B) (8), (10).

43 CX 235 contains similar language.

We also find that respondent made no establishment claims to the effect that Excedrin P.M. relieves more pain than aspirin. None of the ads which represent that Excedrin P.M. relieves more pain than aspirin contains any reference to medical proof.

8. *Claim that Excedrin P.M. is more effective for the relief of nighttime pain than aspirin or any other OTC analgesic.*[44]

We find that respondent did not make this comparative claim. Some of the ads cited by the ALJ do not compare Excedrin P.M. with any other product (e.g. CX 233, 240, 243). Other ads cited by the ALJ state that Excedrin P.M. is a superior product not because it relieves nighttime pain more effectively, but because it contains a sleep-inducing ingredient. For example, CX 228 states:

> Because at night when it's quiet, even a tiny pain can hurt a lot. You could take a simple pain reliever. But it doesn't have anything extra to help you sleep. Excedrin P.M. does. It combines pain relievers with an additional ingredient to gently help you sleep.[45]

There is no indication in this ad that the pain reliever in Excedrin P.M. is special or different from the pain relievers in other products. Furthermore, the evidence in the record confirms that consumers who saw this ad inferred from it that Excedrin P.M. was a product to take at night because it had a sleep-inducing ingredient. (*See* CX 262, 263.) Thus we find that respondent did not represent (and did not represent that it had been established that) Excedrin P.M. is more effective for the relief of nighttime pain than aspirin or any other OTC analgesic.

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44 Complaint paragraphs 7 (B) (9) and 9 (B) (9).

45 Similar ads are CX 229, 235, 236.

C. Required Substantiation for Establishment Claims

1. *Nature of an establishment claim.*

In Part B we found that respondent has represented in its advertisements that the truth of certain superior efficacy and freedom from side effects claims has been established. Paragraph 25 of the complaint alleges that these claims have not been established and that the ads, therefore, are false and misleading and in violation of Sections 5 and 12 of the FTC Act. Bristol-Myers appears to argue that an excessive level of substantiation is being required of it and that complaint counsel are applying a new and different interpretation of the law in this case. (RAB pp. 8-9) In fact, however, the theory is based on the straightforward notion that when an advertiser represents that there is scientific proof or support for a claim, such proof—proof that is generally accepted by the relevant scientific community—must exist.

In previous cases, the Commission has treated similar claims in like manner. For example, in *Porter & Dietsch, Inc.*, we found that claims such as "medically recognized" and "clinic tested" not only implied the existence of substantiation, but they also represented that this substantiation consisted of competent scientific proof. 90 F.T.C. at 865. Similarly, in *Standard Oil Co. of California*, we found that claims of "Here's proof" and "You're about to see proof" clearly invited the assumption that the evidence which followed was based "on tests or other reliable substantiation." 84 F.T.C. at 1472. The Commission went on the conclude that the advertisements "represent that tests had been conducted which proved the claims made in the advertisements." *See also Crown Central Petroleum Corp.*, 84 F.T.C. at 1549. Although the claims in this case (and in the two companion cases) are referred to as "establishment" claims, the underlying legal theory is no different and no more stringent than the theory of the above cited cases.[46]

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46 In this connection, we note respondent's contention that an establishment claim requires only "some basis in fact, or in medical or scientific fact." (R.A.B. p. 47) Respondent has derived this standard from complaint

Of course, we are not committed to the notion that consumers actually understand the details of comparative drug testing. However, consumers have been led by respondent's ads to believe the scientific community regards Bufferin and Excedrin to be superior. For this reason it is necessary to analyze the requisites of establishment for OTC analgesics claims, and determine whether the respondent's evidence does, in fact, establish those products' superiority.

2. *Requisites of Establishment for OTC Analgesic Claims.*

In *Firestone Tire & Rubber Co.*, the Commission concluded that:

> a scientific test is one in which persons with skill and expertise in the field conduct the test and evaluate its results in a disinterested manner using testing procedures generally accepted in the profession which best insure accurate results. 81 F.T.C. at 463.

Thus, the issue is whether the evidence relied upon by Bristol-Myers is generally accepted by the relevant scientific community. The record in this case reveals the elements of proof necessary to establish scientifically an analgesic's comparative superiority. With this perspective in mind, we examine the record and find no reason to alter the decision we reached in *American Home Products* regarding the sort of evidence necessary to substantiate a claim of established superiority for analgesics.

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counsel's witness, Dr. Ivan Ross (Tr. 7008), but we believe it is a misreading of his testimony. Indeed, an examination of his testimony regarding the establishment claims for Bufferin (Tr. 7006-7055) shows that his position is simply that an establishment claim alleges a basis in medical fact (not merely "some" basis), a position which is in accord with our decisions discussed above. It is not entirely clear what respondent means by "some" basis in fact, but even if we accept respondent's characterization of the establishment standard, we believe that it necessarily implies the existence of credible evidence that is probative of the claims in question. As we discuss below, the evidence offered in support of the claims here falls short of that standard.

There is, unfortunately, no way to measure objectively the amount of pain felt by an individual. (Forrest, Tr. 8916) Therefore, the next best method for comparing the effectiveness of analgesics is to elicit the responses of subjects regarding the relief they have obtained after the administration of the analgesics being compared. (Forrest, Tr. 8908-09; Moertel, Tr. 5534) In order to do this, well-controlled clinical tests are conducted in which human subjects report the changes in their symptoms (Azarnoff, Tr. 9179; Grossman, Tr. 7767; Forrest, Tr. 8952, 8908), and this methodology has been employed since the early 1950s, *American Home Products*, 98 F.T.C. at 376. When the goal of the test is to compare the efficacy of two drugs, scientists have normally tested the drugs head-to-head. (Beaver, Tr. 6056; Moertel 5528-29; Forrest, Tr. 8898)

Numerous expert witnesses testified in this proceeding, and there was general agreement among them as to the elements of a well-controlled clinical test. First, the test must involve subjects who are experiencing the appropriate type of pain. In general, the appropriate type of pain is the pain for which the use of the drug is intended. (Evans, Tr. 6353; Moertel, Tr. 5535-36; Forrest, Tr. 8911; Azarnoff, Tr. 9185). If, for example, a claim is made regarding an analgesic's ability to relieve headache pain, at least one of the studies required to establish the claim normally should employ subjects with headaches. (Smith, Tr. 5442) Bristol-Myers challenges this proposition (R.A.B. pp. 66, A.8-A.10) and argues that studies on headache pain are not truly necessary—*i.e.*, "pain is pain." Two of respondent's experts, Drs. Sunshine and Lanman, support this proposition. (Tr. 9754, 12187) Respondent also argues that it is virtually impossible to perform studies on headache pain. However, Bristol-Myers' arguments are weakened by their own witness' testimony. As early as 1968, Bristol-Myers agreed that if studies are to be used to support claims concerning superiority in relieving headache pain, those studies must focus on headache pain. In comments filed in a proposed rulemaking proceeding Bristol-Myers argued that analgesics may function differently in relieving different kinds of pain and that tests on subjects experiencing pain other than headache pain (such as

post-partum pain) are not transferrable. (Lanman, 12013-14)[47] Also, respondent's witness, Dr. Sunshine, testified that FDA guidelines regarding tests of new drugs (guidelines which he assisted in preparing, but with which he claims no longer to agree; Tr. 9824-25) provide that studies should be performed on more than one kind of pain because there is no certainty that the mechanism causing a drug to relieve one kind of pain will be applicable to relief of another kind of pain. (Sunshine, Tr. 9823-25) Taking all this into account and based upon the testimony of complaint counsel's four witnesses, we find that the preponderance of evidence in the record shows that well-controlled clinical tests for measuring an analgesic's comparative efficacy must involve subjects experiencing the type of pain for which the drug is intended. This is in accord with *American Home Products*, 98 F.T.C. at 378.

Moreover, the record does not support Bristol-Myers' contention that studies cannot be conducted on headache pain. Although more difficult to perform because they are outpatient studies (Sunshine, Tr. 9651-52), such studies are feasible and six such studies are mentioned in the record, one of which was performed in 1967. (CX 514, pp. 35382-83)[48] In fact, Bristol-Myers relied on two outpatient studies in this proceeding, one of which examined headache pain. (Lanman, Tr. 11512-17, 12066-67, 12083-84)

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47 Respondent argues that its position in 1968 should not be given much weight because it was not written by scientists but "was written and submitted by Bristol's lawyers in the course of a legal proceeding," and furthermore the lawyers were merely exercising "their lawyer-type efforts . . ." (R.A.B. p. A-10) While we understand the nature of legal advocacy, we note that the position taken by Bristol-Myers in 1968 was based not only upon the efforts of its lawyers, but also upon the opinions of numerous experts including Drs. John Seed, Max Sadove, Louis Lasagna, and Walter Modell. (Lanman, Tr. 12020-26).

48 If such tests were impossible to conduct, this would not necessarily militate in favor of permitting inadequately substantiated claims; at a minimum it would require close scrutiny of secondary sources of support and possible qualification of the claims being made.

With respect to other characteristics of a well-controlled clinical study, the record shows that there should be a written protocol which describes the conduct of the study and its analysis. (Moertel, Tr. 5531, 5542; Azarnoff, Tr. 9180, 9183) Subsequent deviation from the protocol leads to a strong suspicion of bias in the study. (Moertel, Tr. 5542-3) Another possible source of bias is the investigator conducting the study. To minimize this problem, the investigator should generally be both experienced and independent. (Moertel, Tr. 5533-34) Additionally, the persons who administer the test (be they medical personnel or the subjects themselves) should be adequately trained to assure accuracy in recording test results. (Brown, Tr. 4976-77; Moertel, Tr. 5541-42; Forrest, Tr. 8921, 9123-24)

There is virtually no disagreement that test subjects must be randomly assigned to the treatment groups within the study. (Brown, Tr. 4858-60, 4911; Moertel, Tr. 5544; Grossman, Tr. 7768; Evans, Tr. 6342; Forrest, Tr. 8912; Azarnoff, Tr. 9179-80; Laska, Tr. 10166) The purpose of randomization is to make certain that uncontrolled variables are balanced among treatment groups and that subsequently observed differences between treatment groups are attributable to the analgesics being tested and not to the inherent characteristics of the groups. (Beaver, Tr. 6019-22; Forrest, Tr. 8916; Azarnoff, Tr. 9180; Sunshine, Tr. 9864) Failure to randomize the test subjects renders questionable the validity of the study and all subsequent analysis (Brown, Tr. 5083-84; Forrest, Tr. 9114-15), although statistical techniques may be available to correct the imbalance if the importance of the imbalanced variable and the magnitude of the imbalance are not significant. (Brown, Tr. 4911-12, 5086-87, 8052-54; Moertel, Tr. 5544; Forrest, Tr. 9121; Laska, Tr. 10269).

Whenever possible, tests comparing two mild analegesics should also compare those drugs against a pharmacologically inert placebo. (Moertel, Tr. 5539-41; Beaver, Tr. 5979-81; Forest, Tr. 8922; Azarnoff, Tr. 9181) The use of the placebo provides a measure of the study's sensitivity; if the study cannot detect the difference between a standard and the placebo, it cannot be relied upon to detect the difference between

the analgesics being tested. (Moertel, Tr. 5539-41; Beaver, Tr. 5979-80; Forrest, Tr. 8923, 9008-09; Azarnoff, Tr. 9181; Lanman, Tr. 12092-93)[49]

A further typical characteristic of a well-controlled clinical test is double-blinding. That is, neither the test subject nor the person administering the test should be able to tell which treatment is being administered. (Moertel, Tr. 5538; Evans, Tr. 6354, 6357; Grossman, Tr. 7768; Forrest, Tr. 8912; Azarnoff, Tr. 9180; Sunshine, Tr. 9676-77; Laska, Tr. 10166). To achieve double-blinding, it is important that the treatments all look and taste the same. If double-blinding is not used, subjects' responses may be influenced by their own pre-existing biases and by the expectations of those administering the tests. (Beaver, Tr. 6014; Moertel, Tr. 5538; Evans, Tr. 6341, 6357-62)

Respondent objects to the necessity for double-blinding (R.A.B. p. 52, Bristol-Myers Reply Brief p. II-12–II-13), but offers no expert testimony to support its position. First, it argues that it is not a requirement of FDA regulations that double-blinding be used in testing a drug's efficacy, citing 21 C.F.R. 314.111(a)(5)(ii) in support of that proposition.[50] Respondent reads this regulation too narrowly. The regulation states that clinical investigations are essential to support efficacy claims (21 C.F.R. 314.111(a)(5)(ii) and that as part of such an analysis, "methods [must be] used to minimize bias on the part of observers and analysts of the data." (21 C.F.R. 314.111(a)(5)(ii)(a)(4)). The regulations recognize that for certain sorts of tests, double-blinding is not possible or appropriate and other methods must be used to minimize bias.[51]

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49 As we noted in American Home Products, 98 F.T.C. at 377, the rate of response to a placebo is as high as 60% in some studies. We also took note of the placebo effect in Warner-Lambert Co., 86 F.T.C. 1398, 1495-96 (1975), aff'd, 562 F.2d 749 (D.C. Cir. 1977), cert. denied, 435 U.S. 950 (1978).

50 The pertinent parts of 21 C.F.R. 314.111 are identical to 21 C.F.R. 130.12 which was in effect at the time the complaint in this action was filed.

51 For example, double blinding is not possible in a study comparing an oral anagesic with acupuncture. It is not appropriate in a test of a new drug which offers the only chance of survival to terminally ill patients and must, therefore, be administered to all test subjects.

However, in connection with comparative efficacy claims for analgesics, the evidence indicated that double-blinded tests are feasible and appropriate for minimizing bias.

Respondent's second argument is that double-blinding is not appropriate because it will "eliminate the actual and real clinical effect of expectation . . ." (Bristol-Myers Reply Brief p. II-12) We have faced this argument before and rejected it. "The Commission cannot accept as proof of a product's efficacy a psychological reaction stemming from a belief, which, to a substantial degree, was caused by respondent's deceptions." *Warner-Lambert Co.*, 86 F.T.C. at 1496. Indeed, were we to hold otherwise, advertisers would be encouraged to foist unsubstantiated claims on an unsuspecting public in the hope that consumers would believe the ads and the claims would be self-fulfilling.

After the clinical tests are completed, the results should be analyzed to determine their clinical and statistical significance. The procedures for this analysis should be set forth in advance (Moertel, Tr. 5542) and should be adhered to in order to guard against bias caused by a premature conclusion of the study at a time when the data appear to produce a favorable result. (Moertel, Tr. 5542-43) The statistical analysis serves to determine the probability that any apparent differences in efficacy are due to the treatments being tested and are not due to chance. (Brown, Tr. 4867-69; Moertel, Tr. 5545) Scientists generally will accept the differences as being real and not due to chance if analysis shows a 95% level of statistical significance (i.e. there is no greater than a 5% likelihood that the results were produced by chance). (Brown, Tr. 5147; Moertel, Tr. 5545-46; Forrest, Tr. 8912; Azarnoff, Tr. 9182)

Respondent objects to the use of the 95% level of statistical significance to test hypotheses regarding drugs. First, it argues that scientists do not always submit the results of studies comparing drugs to statistical analysis. (Bristol-Myers Reply Brief, p. II-3 – II-4) It is true that when using test results for some purposes (such as determining the proper dosage of a

new drug), scientists do not test statistical significance.[52] However, when those same tests are used to establish the comparative superiority of one drug over another, it is essential to determine the statistical significance of the results (Brown, Tr. 4934-35, 4939, 5137-38; Forrest, Tr. 8899-8901; Sunshine, Tr. 9688-90; Laska, Tr. 10426-28). If this is not done, it is impossible to reject the hypothesis that the drug which may appear superior in the test is, in fact, of only equal (or even lesser) effectiveness.[53]

Respondent's second objection is that even if test results are to be analyzed for statistical significance, the 95% confidence level represents an arbitrary standard. (R.A.B. p. A-2 n.2) This standard, however, was not selected by the ALJ or by the Commission; it was selected by scientists who perform clinical tests on drugs. And, among both complaint counsel's and respondent's experts, there is a consensus that the appropriate level of significance is 95%. (Brown, Tr. 5143; Laska, Tr. 10551-52)[54]

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52 When scientists use a bioassay (see infra pp. 33-34) to determine the proper dose of a new drug, a decision has already been made to use the new drug and the function of the test is solely to determine dosage. They are not concerned with the ability of the study to reject to 95% degree of certainty the hypothesis that the new drug is no more effective than the standard drug against which it is being tested.

53 We reject respondent's argument that the data should be tested against the hypothesis that respondent's products are more effective than others and that if this hypothesis cannot be rejected, the Commission should find no violation. (R.A.B. p. 9-10) Respondent's ads represented that it has been established that its analgesics are more efficacious. The complaint alleges that these claims are false. Thus, to meet its burden of proof, complaint counsel must show that the relevant scientific community does not accept the superiority of respondent's products as proven. Since the weight of expert testimony indicates that comparative superiority can only be established if tests reject the hypothesis that respondent's products are equally effective as others on the market, complaint counsel can meet its burden of proof by showing that tests do not reject that hypothesis.

54 Although the 95% level of statistical significance appears to be necessary to establish unqualified analgesic claims of therapeutic superiority

The next step is to determine whether a statistically significant difference between two drugs is clinically significant. A difference is of no clinical significance if scientists regard the difference as being so small as to be of no importance. (Beaver, Tr. 5971-72)

Finally, in order to establish the comparative efficacy of an analgesic, two well-controlled studies meeting all the criteria set forth above are required. (Brown, Tr. 4878, 8160-61, Moertel, Tr. 5530, 5850-51; Grossman, Tr. 7769; Forrest, Tr. 8917; Azarnoff, Tr. 9185-86) Replication reduces the possibility that the results are due to chance and reduces the effect of flaws in the design of any one study. (Moertel, Tr. 5850-51; Grossman, Tr. 7769; Brown, Tr. 8161; Azarnoff, Tr. 9185). According to Dr. Moertel, replication is especially important for clinical studies of OTC analgesics because of the subjective nature of participants' responses and because of the presence of other variables which are difficult to quantify but could influence test results. (Tr. 5849-51)

As we indicated in *American Home Products*, 98 F.T.C. at 378-381, the criteria set forth above are consistent with regulations adopted by the Food and Drug Administration to implement the 1962 amendments to the Food, Drug, and Cosmetic Act of 1938. (Pub. L. No. 87-781, 76 Stat. 780) These amendments imposed the requirement that there be substantial evidence that a new drug is effective (as well as safe) before it can be introduced on the market. Substantial evidence is defined in the Act to mean:

> evidence consisting of adequate and well-controlled investigations including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded that the drug will have the effect it purports . . . . 21 U.S.C. § 355(d) (1976)

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made to the general public, we note that a lesser standard may be appropriate to support claims that have been adequately qualified or that are made to a limited audience capable of understanding levels of statistical significance.

In promulgating implementing regulations, the FDA pointed out that the criteria necessary to show substantial evidence of a drug's efficacy "have been developed over a period of years and are recognized by the scientific community as the essentials of adequate and well controlled clinical investigations." 21 C.F.R. § 314.111(a)(5)(ii). These criteria include: (1) a clear statement of the objectives of the study; (2) a method of subject selection which minimizes bias, assures suitability of subjects, and assures comparability of pertinent variables; (3) an explanation of observation and recording methods, including steps taken to minimize bias on the part of the subject or observer; (4) a comparison of results with a control; and (5) a summary of methods of analysis and an evaluation of data, including any appropriate statistical methods. 21 C.F.R. § 314.111(a)(5)(ii)(a).[55]

It is the consensus of the experts who testified in this proceeding that at this time well-controlled tests meeting the criteria set out above are necessary to establish comparative superiority for OTC analgesics. However, we recognize that the elements of establishment may change with time. We further recognize (*see* provision I(D) of the order we enter today and p. 67 *supra*) that relevant experts might in some cases regard a proposition as established even if the well-controlled tests did not meet all of the criteria set forth above. But as we discuss below, the evidence possessed by Bristol-Myers was not adequate to establish comparative superiority to the satisfaction of the scientific community.

Respondent further argues that the FDA does not mandate that a proponent of a new drug perform more than one study to establish that drug's efficacy. (R.A.B. p. 52) However, the FDA normally requires at least two tests demonstrating a new drug's efficacy. The regulations provide that a new drug application must include "full reports of clinical *investigations* that have been made to show whether or not the drug is safe

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55 These criteria have been reaffirmed in the FDA procedures adopted in 1972 for reviewing the safety and efficacy of OTC drugs already on the market. 21 C.F.R. § 330 (1979).

for use and effective in use." (21 C.F.R. § 314.1(C) (1980) (emphasis added)). The regulations further provide that a new drug application will be denied if "there is a lack of substantial evidence [of efficacy] consisting of adequate and well-controlled investigations, including clinical *investigations* . . . ." 21 C.F.R. § 314.111(a)(5)(i) (1980) (emphasis added). Thus, the requirement of more than one test is perfectly consistent with FDA regulations.

Respondent additionally contends that FDA regulations do not mandate that study results be tested for statistical significance at the 95% level. It is true that the regulations do not specifically refer to the 95% level of statistical significance. (Nor, for that matter, does the order which we enter today.) However, the regulations do state that the evidence to support a new drug's efficacy must consist of investigations on the basis of which scientific experts could conclude that the drug will have the effect it purports to have. 21 C.F.R. § 314.111(a)(5)(i). The evidence in the record from the expert witnesses provides ample support for the conclusion that scientific experts ordinarily will not draw a conclusion of superior efficacy from a test unless the results of that test are statistically significant at the 95% level. Thus, in effect, the regulations do mandate that test results meet that confidence level, since that is the level of significance relied upon by experts in the field.

Finally, respondent asserts that the standards employed by the FDA to determine drug efficacy should not be applied to comparative performance claims where the basic efficacy of the product is not in question. It argues that FDA regulations must be stringent because they are designed to guard public health and safety by preventing the marketing of ineffective drugs. Once that initial threshold has been crossed, it is no longer necessary to apply such a strict standard to claims of comparative superiority. (R.A.B. p. A-11) Although these FDA standards do not speak directly to the question of comparative efficacy claims, they are entirely consistent with the other evidence, including the considerable expert testimony introduced in this case concerning the kind of support needed to

establish such claims. In addition, the reference to FDA regulations shows the extent to which the criteria for well-controlled tests are widely and uniformly accepted in the relevant scientific community.[56] By contrast, there is little or no evidence in the record of scientific support for an alternative approach. In requiring that establishment claims be substantiated with well-controlled clinical tests, we are not creating a new stringent standard; we are merely applying the standard generally accepted by the scientific community.

D. Evidence of Establishment.

Our analysis of the advertisements in Part B above showed that respondent had represented that it has been established that:

1) Bufferin relieves pain faster than (and in some ads, twice as fast as) aspirin;

2) Bufferin will upset a person's stomach less frequently than aspirin;

3) A dose of Excedrin relieves more pain than (and in some ads, twice as much pain as) a dose of aspirin;

4) Excedrin is a more effective pain reliever than aspirin or any other OTC analgesic (and in some ads, more effective because it has four indgredients).

We must now determine whether these claims have been established—that is, whether the respondent's establishment representations are correct.

1. *Claims regarding Bufferin's speed.*

Respondent has supplied no clinical evidence in support of claims regarding the speed of analgesia (pain relief) provided by Bufferin. Instead, it has supplied numerous studies which

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56 Although we are only using FDA regulations as one indication of what experts require before they will regard a claim of superior efficacy as established, we note that in 1979 the same standards set forth in 21 C.F.R. § 314.111(a)(5) were made applicable to comparative safety and efficacy claims made in prescription drug advertising. 44 Fed. Reg. 37434, 37466-67 (June 26, 1979).

show that Bufferin is absorbed into the bloodstream twice as fast as aspirin. (F. 566-583) There is little question that an analgesic must be absorbed into the blood before it can begin to relieve pain. However, according to all of the experts who testified in this case, it has yet to be shown that there is a correlation between the rate of absorption of an analgesic into the blood and the rate of onset of pain relief. (Moertel, Tr. 5801-05, 5817-18, 5860; Beaver, Tr. 5945-46; Forrest, Tr. 8987-90; Azarnoff, Tr. 9189-90) It may appear logical to infer speed of relief from speed of absorption, but complaint counsel's experts agree that such an inference is at best a hypothesis which must remain a hypothesis until proven in well-controlled clinical tests. No data exists to prove that inference. As Dr. Beaver stated, "The problem with analgesics is that that data just isn't there and there are certain data which suggest that this correlation is not at all simple." (Tr. 5952; *see also* Moertel, Tr. 5800-06, 5817-18, 5860; Beaver Tr. 5947-48, 5957-58, 5961-64; Forrest, Tr. 8980, 8987-90, 9035, 9043-45; Azarnoff, Tr. 9195, 9225)

Respondent's only witness in support of Bufferin's superior speed was Dr. Lanman, the former medical director of Bristol-Myers, who was not qualified as an expert in the area of pharmacokinetics. His testimony in this proceeding was contradicted by a memorandum he wrote in 1969 which admitted that there was no known correlation between the rate of an analgesic's absorption and the rate of onset of analgesia. Furthermore, in 1967, the National Research Council, a subsidiary of the National Academy of Science, reviewed Bristol-Myers' substantiation for the claim that Bufferin provides pain relief faster than aspirin and found that the claim was "ambiguous and misleading." The report also found that there was "no evidence" that Bufferin provided significantly faster relief than aspirin. (CX 511F)[57] This same claim was considered by

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57 The NAS/NRC panel was composed of a number of well-known experts in the field of pharmacology (Beaver, Tr. 5903), and it operated under the aegis of the FDA. Its purpose was to evaluate the efficacy of drugs that had been introduced on the market prior to 1962. In 1972, the Panel's findings were published in the Federal Register. (Beaver, Tr. 5899; Tr. 5925)

the FDA's Advisory Review Panel on OTC Analgesics after reviewing extensive submissions from Bristol-Myers. (Lanman, Tr. 12115-16; CX 506) The Panel concluded that it was

> unaware of any data that demonstrate that buffered aspirin [such as Bufferin] provides a more rapid onset, a greater peak of intensity or a more prolonged duration of analgesic effectiveness than unbuffered aspirin. (CX 514 at 35378)[58]

Respondents argue that the FDA OTC Analgesics Panel found several analgesics to be effective based solely upon blood absorption data (R.A.B. p. 49). This argument appears to us to be irrelevant. While the Panel may well have considered blood absorption data for some purposes, it is clear that they did not find it adequate to demonstrate a more rapid onset of analgesia for Bufferin. The fact is that many experts (including those on the FDA OTC Panel) have considered the blood absorption studies offered by Bristol-Myers and have not been able to conclude that Bufferin provides faster relief from pain than aspirin. That is the issue before us here. Thus, we cannot conclude respondent's claims of superior speed of pain relief have been established. Since it has not been established that Bufferin provides faster pain relief than aspirin, it has also not been established that it provides pain relief twice as fast.

2. *Claims that Bufferin will upset a person's stomach less frequently than aspirin.*

Some individuals suffer gastric intolerance to aspirin (*see* p. 55 infra) and, in certain instances, doctors prescribe that these individuals take antacid in conjunction with aspirin in order to reduce the chances of stomach upset. This is the theory behind the formulation of Bufferin which contains 5 grains of aspirin and about 150 mgs. of antacid. Dr. Morton Grossman, complaint counsel's expert in the field of gastroenterology stated

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58 This view is also shared by the experts who prepared the *AMA Drug Evaluations* (CX 512H, 518G).

that, "the small amount of buffering that is present in Bufferin . . . would not be expected to have any effect upon the secreted acid in the lumina of the stomach." (Tr. 7772) Furthermore, he indicated that if a patient were suffering gastrointestinal problems from aspirin, he would "place the patient on a full antacid regime to be taken along with the aspirin," and he would prescribe a dosage of antacid 75 times larger than that contained in Bufferin. (Tr. 7773-74) In addition, he noted that the antacid in Bufferin would have no effect on stomach upset which occurs after aspirin enters the blood. (Tr. 7772-73) Finally, he stated that only well-controlled clinical studies could establish that Bufferin causes less stomach upset than aspirin. (Tr. 7769-71) Thus, the composition of a Bufferin tablet and the speed with which it enters the blood do not establish that Bufferin causes less stomach upset than aspirin.

Bristol-Myers presented no expert testimony in support of Bufferin's freedom from side effects but did supplement the evidence regarding chemical composition and speed of absorption with four studies comparing Bufferin's side effects with aspirin. However, none of these studies is a well-controlled clinical study. Two of those studies use a historical control (the Paul Study, CX 786, and the Tebrock Study, *see* Lanham, Tr. 11478, 11486), which means that the subjects were given Bufferin and then asked to compare its side effects with what they remembered to be the side effects associated with aspirin. It is impossible to know whether the test subjects accurately remembered and related past experiences with aspirin or whether they were able to distinguish the side effects caused by aspirin from side effects generated by other possible causes. As further evidence of the inappropriateness of this method of testing, FDA regulations permit historical controls only where it would be unacceptable to leave the disease being studied untreated or to treat it by a means other than the test treatment. 21 C.F.R. 314.111(a) (5) (ii) (a) (4).[59] Also, Dr. Gross-

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59 Respondent's witness Dr. Lanman argues that although the methods used to conduct these two tests might not be appropriate now, they were appropriate in 1949 and 1952 when the tests were conducted. (Lanman, Tr. 11477-78) However, by the 1960s, other methods of testing had been

man indicated that he would reject the two studies because they "were open trials without randomization and without double-blind controls." (Tr. 7961)

The third study presented by Bristol-Myers, the Fremont-Smith Study, was also flawed. Subjects were not randomly assigned to treatments and aspirin was given to most of them first. This failure to randomize the order can produce "very, very misleading" results (Laska, Tr. 10433) due to the physiological and psychological "carry over" problems where only one drug is given during a particular period of a test. Furthermore, the test patients were arthritis sufferers, many of whom were subject to a variety of gastric abnormalities. (Lanman, Tr. 12050) Thus, even if this test had been well-controlled, it would be generalizable only to those suffering similar abnormalties.

The fourth study, the Sher Study, was conducted in a prison and was never published. (Lanman, Tr. 12054, 12061) Evidence regarding the claim of less stomach upset was reviewed in 1967 by the NAS/NRC Panel (the Sher Study was among the studies they considered) and the Panel concluded that it indicated little difference in the incidence or intensity of side effects from Bufferin or plain aspirin. (CX 511F) The same conclusion was reached in *AMA Drug Evaluations* (CX 512, 518) and by the FDA OTC Analgesics Panel. Thus, the record shows that it has not been established that Bufferin causes less stomach upset than aspirin.

3. *Claims regarding Excedrin's superior efficacy.*

Respondent presented three types of evidence relating to Excedrin. The first relates to Excedrin's formula. Excedrin contains 3 grains of aspirin, 1.5 grains of acetaminophen, 2 grains of salicylamide, and 1 grain of caffeine. We agree with the ALJ's finding (F. 478) that the number and quantity of

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developed (supra p. 24) and were being used by experts in the field of pharmacology. What is relevant in this case is whether the claims regarding Bufferin, in light of available learning, were established at the time they were made in the late 1960s and early 1970s. It thus seems clear in this case that tests done 20 years earlier could not establish those claims.

ingredients in an analgesic is not evidence alone which can establish the superiority of one product over another. There must be some demonstration of or explanation for the differences. Indeed, complaint counsel's witness Dr. Forrest, an eminent expert in the field of clinical testing of analgesics, stated that adding ingredients may work to the betterment of a drug but may also work to its detriment. Only good clinical data can support the proposition that more is better. (Tr. 8977-78) In fact, Excedrin contains only 4.5 grains of ingredients recognized as analgesics (aspirin and acetaminophen) compared to a normal 5-grain aspirin tablet. Furthermore, the FDA OTC Analgesic's Panel concluded that the amount of salicylamide in Excedrin is ineffective as an analgesic. (CX 514, p. 35441) Caffeine, also, has not been established as an analgesic and its value as an adjuvant (i.e., an ingredient that assists) to aspirin and acetaminophen is unclear. (Forrest, Tr. 9107) The studies presented by respondent regarding caffeine's value are at best ambiguous (F. 477) and the FDA OTC Analgesic's Panel considered much of the evidence presented in this case by Bristol-Myers and was unable to conclude that caffeine contributed an adjuvant effect. (CX 514, p. 35441, 35484)

The second type of evidence regarding the Excedrin claims consists of a study based upon experimentally induced pain, the Sherman study (CX 439). This study compared the ability of Excedrin and aspirin to raise the threshold at which subjects could first feel pain caused by an electric shock to their tooth pulp. The major problem with this study is that results relating to pain induced experimentally are not considered to be applicable to naturally occurring pain. This is the opinion expressed in the writings of Drs. Beecher, Chapman, and Mumford, all of whom were recognized as experts by respondent's witness Dr. Elvers. (Elvers Tr. 11111, 11166, 11163-64) Indeed, the methods employed by Dr. Sherman produced results that were inconsistent with clinical literature, with clinical tests, and with bioassay studies. (F. 545) Furthermore, in the draft report of the Sherman Study, the authors recognize the limited applicability of the study when they state "aspirin might be more

effective in relieving other types of pain" than that induced by electric shock to tooth pulp. (CX 450G) At the instruction of Dr. Elvers (who was then Associate Medical Director of Bristol-Myers Product Division), this statement was omitted from the final version of the report. (CX 449D) Nevertheless, in the final version of their report, the authors still admit that the results of their study may be limited to types of pain similar to the type being studied (CX 439L), and respondents concede this point. (RAB p. A2)

The Sherman Study also suffered from methodological flaws which were described in some detail by Dr. Evans, complaint counsel's witness, who was qualified in this proceeding as an expert in pain, experimental pain and the response of pain to treatment. (F. 33) First, the study measured only the ascending threshold of pain rather than averaging the ascending and descending thresholds, which is considered the appropriate scientific procedure. (Evans, Tr. 6377) Indeed, Dr. Wolff, an expert in experimental pain research recognized by Dr. Elvers, agrees that the ascending and descending thresholds must be averaged. (Elvers, Tr. 11140) Second, the Sherman Study tested the subjects' pain threshold only, rather than measuring the supra-threshold (point at which pain becomes intolerable). Both Drs. Evans and Wolff regard tests of the supra-threshold as a better indicator of analgesic efficacy than the pain threshold because the supra-threshold is more likely to be affected by analgesics. (Evans, Tr. 6382-85; Elvers, Tr. 11127) Third, Dr. Sherman eliminated 30% of the subjects from the test without gathering data on these subjects, which is considered to be an unacceptable procedure. (Evans, Tr. 6395; CX 439C) Fourth, Dr. Elvers was unable to explain fully the fact that large amounts of electrical current (in one instance, more than 300 times the normal amount) were required to reach the subjects' pain thresholds. (Tr. 11212-36) Finally, Bristol-Myers was unable to replicate the results of the Sherman Study. (Elvers, Tr., 10897-10901)

Although respondent refers to eight other studies using experimental pain (R.A.B. p. A1, A2; Bristol-Myers Reply Brief p. II-7 - II-8), none of these studies was introduced into

evidence and none was evaluated by the various experts who testified in this proceeding. Thus, these studies do not establish Excedrin's superiority.

The third type of evidence submitted by Bristol-Myers consists of two bioassays; one performed by Dr. Emich and the other by Dr. Smith. It is this evidence that comes closest to establishing the claims regarding Excedrin. A bioassay is a study of complex design whose purpose is to determine the amount of a test drug necessary to equal the analgesia produced by a standard drug (in this case, aspirin). The result of a bioassay is the "relative potency" of the test drug. (Brown, Tr. 4849; Forrest, Tr. 8884) The relative potency of two drugs is different from their relative efficacy. Relative potency produces a conclusion about the amount of a test drug necessary to produce a desired amount of analgesia; relative efficacy is a comparison of the effectiveness of equal doses of the test drug and the standard drug. (Brown, Tr. 4853-54; Laska, Tr. 10417) Although a bioassay is normally used to draw conclusions about relative potency, its results may also be used to compare the efficacy of drugs. (Forrest, Tr. 8885-8807; Laska, Tr. 10487) However, when using the results of a bioassay to compare efficacy, the data must be analyzed in a different fashion than if the data are used to determine relative potency. When determining drug dosage, scientists are interested in the "best estimate" of relative potency. (Sunshine, Tr. 9670, 9689; Laska, Tr. 10206-08) Both respondent's and complaint counsel's experts agree that when comparing efficacy (and attempting to show the superior efficacy of one drug over another), scientists analyze the data to determine whether the possibility that the drugs are equally efficacious may be excluded. (Forrest, Tr. 8899-8902; Brown, Tr. 8078; Laska, Tr. 10426-27, 10519-25)[60]

Respondent argues repeatedly and strenuously about the appropriate method of analyzing the results of a bioassay. (R.A.B. pp. 5, 9, 12 n.1, A5-A6) Respondent contends that scientists do make use of and do draw conclusions from

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60 As explained above, this is the appropriate hypothesis to test because Excedrin's advertising claimed that Excedrin was more efficacious.

bioassay results in which the possibility of equal efficacy has not been excluded to a 95% degree of certainty. To support this, they refer to no expert testimony but do cite a published article reporting the results of a bioassay performed by complaint counsel's expert witness Dr. Brown, entitled "Assay of Aspirin and Neoproxin Analgesia." (R.A.B. p. A.5 - A.6) In this bioassay, a conclusion was drawn from the data even though it was not possible to reject the possibility of equipotency to a 95% degree of certainty. Thus, respondent contends that for purposes of substantiating advertising claims regarding Excedrin, the bioassays should not be subject to statistical analysis. Respondent has failed to distinguish between the two uses to which bioassays may be put. The primary purpose of a bioassay is dose selection—the recommended dose must be determined for a new drug. This was the purpose of the bioassay performed by Dr. Brown. If the confidence interval surrounding the best estimate of relative potency is not too large, that best estimate will be used to recommend a dose. (F. 428-429) Scientists normally do not use bioassays to compare the efficacy of analgesics. (Laska, Tr. 10405-07) However, when they do, they then analyze the results to determine whether they can reject the possibility that the drugs are equally effective. The record contains only one example of a published bioassay used to compare efficacy. The article was authored primarily by Dr. Louis Lasagna (respondent's expert Dr. Laska is listed as a co-author) and it states that the results of the bioassay do not permit a conclusion of differing efficacy because it was not possible to reject the hypothesis of equal efficacy to a 95% degree of certainty. (Tr. 10521-22) Furthermore, substantial expert testimony in the record supports the conclusion that this is the proper method of interpreting bioassay results when attempting to draw a conclusion regarding comparative efficacy. (Brown, Tr. 4934-35; Forrest, Tr. 8899-8901; Laska, Tr. 10426-27)

The Smith Study is a bioassay on patients suffering post-partum pain which compares three doses of Excedrin, aspirin, and a placebo. The author of the study, Dr. Smith, stated that he did not believe his study showed any statistically significant difference between Excedrin and aspirin. (Tr. 5422-24) How-

ever, respondent contends it supports Excedrin's superior efficacy. As in most bioassays, the performance of the products was assessed by measuring the reduction in the subjects' pain intensity at various time intervals after administration of the drugs and by measuring the amount of pain relief they received during the same intervals. (F. 406-409) The Smith Study was well-controlled and well-designed in all respects. (Brown, Tr. 8150) For all six parameters analyzed in the study, Excedrin showed a relative potency slightly exceeding 1.0 (meaning that a somewhat smaller dose of Excedrin was necessary to produce the same amount of analgesia as a given dose of aspirin). However, as explained above, in order to compare effectiveness, the data have to be tested against the hypothesis of equal effectiveness, and for all six parameters, the data showed that it was impossible to reject, to a 95% degree of certainty, the possibility that Excedrin and aspirin were equally effective. (Indeed, the data were so equivocal that for four of the six parameters it would be impossible to reject the hypothesis that Excedrin was only two-thirds as effective as aspirin.) According to Dr. Brown, who was qualified as an expert biostatistician in this proceeding, the results of the Smith Study are quite consistent with the results that would be obtained in a bioassay where the true relative potency of the two compounds was, in fact, equal. (Brown, Tr. 5009, 8157-58)

Respondent cites Dr. Laska (an expert in the testing of analgesics) in support of the proposition that the Smith Study is acceptable evidence that Excedrin is stronger than aspirin. (R.A.B. p. A5) However, what Dr. Laska actually says is that the Smith Study cannot be used to reject the hypothesis that Excedrin is more effective than aspirin. (Tr. 10295) He later also concedes that the Smith Study does not reject the hypothesis that Excedrin and aspirin are equally effective (Tr. 10518), and Dr. Sunshine, respondent's expert in clinical pharmacology drew the same conclusion (Tr. 9751). Finally, Dr. Laska states that his experience does not permit him to generalize the results of the Smith Study to any kind of pain other than post-partum pain. (Tr. 10306-07)

The second bioassay submitted by respondent was the Emich Study. (The study was also performed exclusively on women suffering from post-partum pain.) The Emich Study was a less

reliable estimate of relative potency than the Smith Study because it employed fewer subjects and was methodologically flawed. (Brown, Tr. 8150) The same six parameters that were analyzed in the Smith Study were analyzed by Emich and they showed a relative potency ranging from 2.27 up to 7.1 (meaning that Excedrin ranged from 2.27 to 7.1 times as potent as aspirin). (F. 484) However, statistical analysis showed that for three of the six parameters, the Emich Study was unable to reject the hypotheses that Excedrin was equally or less potent than aspirin. Nevertheless, Dr. Laska, respondent's statistician, stated that the Emich Study provided "compelling evidence of superiority" of Excedrin over aspirin (Tr. 10185), and Dr. Sunshine, respondent's expert in clinical pharmacology, stated that the Emich Study gives "strong scientific evidence that Excedrin is stronger and more effective than aspirin on a tablet for tablet basis." (Tr. 9660)[61]

The major flaw in the Emich Study was baseline pain imbalance. More patients initially having severe pain were assigned to the group given Excedrin. (Brown, Tr. 5174; Sunshine, Tr. 9662) The authors of the Emich Study noted that "the response of an individual patient to a given medication was closely related to her starting level." (CX 425N) This means that Excedrin had a greater opportunity to relieve pain than did aspirin. (Brown, Tr. 4904, 5174) For this reason, respondent's expert Dr. Laska admitted that he would have no confidence in using those parts of the data from the Emich Study which measured the reduction in subjects' pain intensity. (Laska, Tr. 10440)

To overcome this problem, the authors of the Emich Study performed a *post hoc* statistical analysis to correct for the initial pain imbalance. (In fact, two of the three parameters which rejected the hypothesis of equal effectiveness were produced in this analysis. The third parameter was a measure of reduction in pain intensity in which even Dr. Laska would have

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61 Dr. Sunshine's subsequent testimony, however, indicates that he was not concerned with whether the Emich Study could be used to reject the hypothesis that Excedrin and aspirin are equally effective. (Tr. 9863-77)

no confidence.) In the opinion of respondent's statistician, this analysis corrects the imbalance. (Laska, Tr. 10199-10201) However, Dr. Laska conceded that if the subjects in the study were not assigned to treatment groups in an unbiased fashion, the entire study would be seriously compromised. (Tr. 10590-94) And because he felt such bias was present, complaint counsel's statistician Dr. Brown stated that the *post hoc* analysis was inappropriate. Indeed, the record shows that if true randomization had been present in the Emich Study, the baseline pain imbalance would occur only 2% of the time. (Brown, Tr. 4903, 4921; Forrest, Tr. 8960) Because of this imbalance, both Drs. Forrest and Brown concluded that they would not rely on the Emich Study as credible evidence regarding the superiority of Excedrin over aspirin. (Brown, Tr. 8108, 8149-50, 8154-55; Forrest, Tr. 8960-61, 9121-23)[62]

Finally, even accepting respondent's attempts to correct for methodological flaws, the resuts are, at best, equivocal in that for some parameters the Emich Study rejects the hypothesis of equal effectiveness and for others it does not. (F. 500) In part to compensate for this, respondent combined the results of the Emich and Smith Studies in order to produce another analysis of their results. However, pooling the two studies does not produce a third study; it merely reduces two independent studies into one. (Brown, Tr. 8159-63; Forrest, Tr. 8965-68) Not surprisingly, the results of the pooled study are also equivocal and are able to reject (just barely) the hypothesis of equal effectiveness for only two of the five parameters. (F. 521)

In order to establish that Excedrin is a more effective pain reliever than aspirin, scientists require the proposition to be demonstrated by two well-controlled clinical tests. The Smith

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62 The testimony shows that there was only one published analgesic study (the Emich Study was not published when its authors failed to answer adequately a question regarding its applicability to other types of pain (Lanman, Tr. 12095-97)) in which there was significant baseline pain imbalance and the author of that study, Dr. Louis Lasagna (who was cited by respondent in its 1968 comments to the F.T.C. (Lanman, Tr. 12023-24)) indicated that because of the imbalance he could come to no conclusion about the tested drugs. (Laska, Tr. 10626-27)

Study is such a well-controlled study but for all parameters analyzed, it could not reject the hypothesis of equal effectiveness. Since it was done on post-partum pain, respondent's statistician stated that its result were not generalizable. The Emich Study was also performed on post-partum pain and its authors also admit that its results are not generalizable to other forms of pain (such as headache pain for which Excedrin is promoted). Furthermore, this study was less well-controlled than the Smith Study creating questions of bias in the initial assignment of patients. Although these two studies may present some evidence of Excedrin's superiority, they clearly are unable to establish it. The additional nonclinical evidence submitted by respondent also does not establish superiority.[63]

E. The Substantial Question Issue

The second set of allegations related to respondent Bristol-Myers' comparative performance claims is contained in paragraphs 9-11 of the complaint. These paragraphs set forth the same 15 comparative performance claims contained in paragraph 7 and allege that even in those instances in which the ads did not indicate that the truth of the claims had been established, respondent violated the law by failing to disclose the existence of a substantial question as to the claims' validity. The complaint also alleges that respondent failed to disclose the existence of a substantial question regarding the validity of two additional claims contained in paragraph 14.[64] Although a

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63 The evidence submitted by respondents compared Excedrin only to aspirin. Thus, there is no evidence comparing Excedrin to all other OTC analgesics and it has not been established that Excedrin is superior to them in any respect.

64 Complaint paragraph 14A alleges that respondent advertised that tests or studies prove that Bufferin is twice as fast and twice as strong as aspirin. As we indicated in Part B, (supra pp. 9-11), ads such as CX 31, 61, 63 and 64 state that tests show Bufferin is twice as fast as aspirin. The ALJ found no ads which state Bufferin is twice as strong as aspirin and we agree with that finding. Paragraph 14B alleges that respondent advertised that tests or studies prove Excedrin is more than twice as strong and more effective than aspirin in relieving pain. As we indicated in Part B (supra pp. 16-18),

majority of the Commission found that respondent in *American Home Products* had violated the law by failing to disclose the existence of a substantial question with respect to certain claims, we have reconsidered that theory of liability and can no longer endorse it. For that reason, we dismiss all allegations in paragraphs 9-11 and 14-16 of the complaint.

The "substantial question" doctrine (and our reasons for rejecting it here) can best be understood by comparing it to the "reasonable basis" standard enunciated in *Pfizer, Inc.*, 81 F.T.C. 23 (1972). In *Pfizer*, the Commission ruled that it was an unfair act or practice for an advertiser to make a claim without having a reasonable basis for believing that the claim was true. The amount of evidence required to provide a reasonable basis was left to be determined on a case-by-case basis, for the Commission recognized that the reasonableness of an advertiser's supporting evidence would depend on a number of factors. Among the factors recognized as relevant in the *Pfizer* opinion were:

> (1) the type and specificity of the claim made—*e.g.*, safety, efficacy, dietary, health, medical; (2) the type of product—*e.g.*, food, drug, potentially hazardous consumer product, other consumer product; (3) the possible consequences of a false claim—*e.g.*, personal injury, property damage; (4) the degree of reliance by consumers on the claim; (5) the type and accessibility of evidence adequate to form a reasonable basis for making the particular claim.[65]

Excedrin ads do claim that studies show Excedrin is more effective than aspirin. (E.g. CX 205, 206) Also Excedrin ads state that it would take more than twice as many aspirin to equal the pain relief of Excedrin. (E.g. CX 176) Although ads such as this do not actually state that Excedrin is more than twice as strong as aspirin, consumers would reasonably infer this. Thus, we find that respondent made the claims alleged in paragraph 14B and part of the claim alleged in 14A.

65 Pfizer, Inc., 81 F.T.C. at 64. In subsequent decisions, we ruled that it was legally deceptive (as well as unfair) for an advertiser to make a claim without a reasonable basis, because consumers *expected* advertisers' claims to be supported by a reasonable basis. See infra pp. 41-42.

However, in *American Home Products Corp.*, 98 F.T.C. 136 (1981), the Commission took a somewhat different approach to the relationship between an advertiser's claims and the evidence supporting them. That case, like this one, involved claims that an analgesic possessed properties which had not been established by generally acceptable scientific evidence. The case might have been pled and argued on the theory that, under the criteria set forth in *Pfizer*, only generally acceptable scientific evidence (i.e., two well-controlled clinical tests) would suffice to provide a reasonable basis for such claims. However, this was not the theory on which the case was argued or decided. Instead, what the Commission actually ruled was that the absence of such scientific evidence created a "substantial question" about the truth of the advertiser's claims—and that the existence of this substantial question was a material fact which consumers ought to know. Making such claims without disclosing the absence of authoritative scientific proof was therefore deemed legally deceptive.

This theory of liablility was subsequently upheld by the Third Circuit in *American Home Products Corp.* v. *FTC*. In reasoning similar to that used by the Commission, the court emphasized that consumers could not judge for themselves the effectiveness of competing pain relievers, that drugs were heavily regulated as to safety and efficacy by the federal government, and that American Home's advertising campaign was so intensive and long-lasting that consumers might well come to believe that the claims being made had been established as a matter of scientific proof. Thus, while the court was reluctant to assume that consumers expected *every* analgesic claim to be backed by scientific proof (695 F.2d at 697-699), it ruled that the Commission could reasonably infer that consumers had expected such proof in the case of American Home's claims.

The practical difficulty with this doctrine, however, is that it is difficult to see where it stops. In effect, the substantial question doctrine elimates any difference between the claim, "Our product works better than aspirin," and the claim, "Scientific tests *prove* that our product works better than aspirin." It has always been recognized that the latter claim is deceptive if the scientific tests referred to in the claim do not

exist, or do not prove the truth of the claim. Under the substantial question doctrine, though, the former claim must also be proven with the same level of scientific evidence, or it will be deemed deceptive for failure to disclose the existence of a "substantial question" regarding the truth of the claim. The level of proof that is legally required will thus be the same whether the advertisement specifically refers to scientific proof or not.

There might, of course, be cases where consumers do in fact interpret both of the above claims as implying the same level of scientific certainty. The presence or absence of any reference (express or implied) to scientific tests would then be irrelevant, if consumers interpreted the claim the same way in either case. The difficulty, however, is that there has never been any evidence to confirm this somewhat counterintuitive reading of consumer expectations. The factors relied on by the Commission in *American Home Products*—i.e., the pervasive regulation of drug safety and efficacy, and the fact that consumers cannot judge such issues for themselves—would apply with equal strength to *every* drug claim.[66] If these factors alone are enough to warrant an inference that consumers expect authoritative scientific proof for a claim, then there is no way to avoid drawing a similar inference in every other drug case (where the same factors will always be present), and the Third Circuit's concerns about an across-the-board application of the substantial question doctrine would be realized.

Thus, we are not ruling out the possibility that, in some future case, a proper showing might be made that consumers did expect unequivocal scientific proof even when the advertisements made no express or implied reference to such proof. We decline, however, to impute such expectations to consumers solely on the basis of the general characteristics of the drug

66 We also question the notion that an advertiser should be held to a higher standard of proof if it has made claims in a large number of advertisements over a long period of time. An intensive and long-lasting campaign is probably more likely to be remembered by consumers, and may well be more effective for that reason. Consequently, the duration of the campaign may be relevant to the need for a corrective advertising requirement (see infra pp. 75-76), or to other issues concerning the appropriate scope of a cease and desist order. However, there is no evidence at all to suggest that consumers expect a higher level of proof in long-lasting campaigns than in other contexts.

market such as pervasive regulation or consumers' inability to test the claims themselves. To this extent, our decision here departs from our prior ruling in *American Home Products*.

Instead, we hold today that such cases ought to be judged (absent stronger evidence of some higher level of consumer expectations) under the "reasonable basis" standard of *Pfizer*. We thus are not ignoring the fact that there is also a difference between the claim, "Our product works better than aspirin," and the claim, "We think our product works better than aspirin but we have no proof of it." *See American Home Products*, 98 F.T.C. at 387. The latter claim implies virtually no supporting evidence; the former implies that the advertiser has at least some measure of support for the claim. But unless we have more direct evidence of what measure of support consumers actually expect, the measure that would be appropriate (or "reasonable") can only be determined by reference to factors such as those discussed in the *Pfizer* opinion.

This conclusion is entirely consistent with the Commission's other post-*Pfizer* substantiation decisions. While we have often ruled that the failure to possess a reasonable basis can be deceptive as well as unfair (on the grounds that consumers expect advertisers to possess a reasonable basis), we have never tried to set the measure of a reasonable basis exclusively directly by reference to consumers' expectations. As we said in *National Dynamics Corp.*, 82 F.T.C. 488, 550 n. 10 (1973), *aff'd in part, remanded in part*, 492 F.2d 1333 (2d Cir. 1974), *cert. denied*, 419 U.S. 993 (1974):

> [P]erformance claims lacking a reasonable basis in fact may be found deceptive within the meaning of Section 5 of the F.T.C. Act. . . . Whether an advertisement is analyzed from the standpoint of unfairness or deception, however, the standard for evaluating the substantiating material and test which is applied is the same—does the substantiation provide a reasonable basis to support the claim.[67]

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67 See also Porter & Dietsch, Inc., 90 F.T.C. 866 at n.11; National Comm'n on Egg Nutrition, 88 F.T.C. 191 at n.14.

Had such an analysis been performed in this case, it might well have led to the conclusion that a reasonable basis for these claims would in fact have required two well-controlled clinical tests. That is, the *Pfizer* analysis might well have led to the same conclusion as the "substantial question" doctrine, and provided an independent basis for finding a violation here.[68] Certainly the fact that consumers cannot judge analgesic claims for themselves would be one factor to take into account in that analysis, along with such other factors as the cost of testing, the extent to which lower levels of testing would reduce the certainty that a claim that survived the tests was in fact true, and the extent of the injury consumers would suffer if the claim turned out not to be true.[69] However, the difficulty with this rationale is that no such analysis has been conducted in this case. The complaint did not allege that Bristol-Myers' comparative claims were not supported by a reasonable basis, and the parties did not argue the case on that theory either before the Commission or before the ALJ. That issue therefore is not properly before us, and we are unable to rule on that theory of liability.

In short, on the record before us we can only find that the failure to possess two well-controlled clinical tests in support of a claim of comparative superiority violated the FTC Act when the advertisement in some way referred to or implied the existence of scientific proof. This approach is in accord with a long line of previous Commission decisions. For example, in *Firestone Tire & Rubber Co.*, 81 F.T.C. 398 (1972), we required the respondent to substantiate its claims with scientific tests

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68 The Pfizer opinion itself acknowledged such a possibility, noting that "there may be some types of claims for some types of products for which the only reasonable basis, in fairness and in the expectations of consumers, would be a valid scientific or medical basis." 81 F.T.C. at 64.

69 Pfizer, Id. In some cases, the benefits consumers would receive if the claim were in fact true may also be relevant (especially if they are far greater or far less than the harm consumers would suffer if the claim turned out to be false), as this will affect the cost of setting too high or too low a standard of evidence.

because its advertisements represented that its 25% quicker stopping claim was backed by scientific tests. (Indeed, respondent conceded that such representations had been made. 81 F.T.C. at 450.) Similarly, in *Standard Oil Co. of California*, the advertisements in question contained white-jacketed technicians performing a demonstration and used such phrases as "Here's proof" and "You're about to see proof." 84 F.T.C. at 1472. In *Litton Industries, Inc.*, 97 F.T.C. 1 (1981), we required Litton to substantiate its claims with competent and reliable surveys or tests because its ads mentioned surveys and tests, thereby implying a measure of support for the claims which did not exist. Finally, in *National Commission on Egg Nutrition*, we required respondent to disclose the existence among medical experts of a substantial question regarding the relation of egg consumption to heart attacks. 88 F.T.C. at 193. However, respondent had represented in its ads that scientific evidence supported the view that eating eggs was safe. In each of the above cases, we required the respondent to substantiate advertising claims with particular kinds of proof (or to disclose that the proof was not as one-sided as represented) because the ads in question represented that the proof existed.[70]

We apply the same test in this case. Numerous ads for Bufferin and Excedrin represent that there exists scientific

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70 In Simeon Management Corp., 87 F.T.C. 1184 (1976), aff'd, 579 F.2d 1137 (9th Cir. 1978), we found it to be deceptive for an advertisement to omit the fact that the drug used in the advertised course of treatments had not been approved as safe and effective for that purpose by the FDA. However, even in that case there had been affirmative claims which the respondent conceded represented that the treatment had been "medically approved." 87 F.T.C. at 1230; see also Id. at 1208 ("Lose weight safely . . . through our *proven* weight reduction program") (emphasis added). Moreover, in Simeon the omitted fact did not relate merely to the level of substantiation possessed by the advertiser, but rather to the absence of formal governmental approval (approval which would have been legally required had the drug been marketed directly rather than as part of a treatment program). In this case, Bristol-Myers' products have all been approved by the FDA as safe and effective for their advertised purposes—and if that had not been the case, the failure to disclose that lack of approval would clearly be deceptive under Simeon.

proof establishing the product's superiority. As we discussed above in Parts B, C and D, these claims must be substantiated by two well-controlled tests. For all non-establishment superiority claims, we dismiss those portions of the complaint which allege that respondent failed to disclose the existence of a substantial question among experts regarding the validity of such claims. Although our order includes a reasonable basis requirement for non-establishment analgesic claims, we decline to conclude at this time that two well-controlled clinical tests constitute the only acceptable substantiation for these claims.

III TENSION RELIEF CLAIMS

Complaint paragraph 12 alleges that Bristol-Myers represented that Bufferin, Excedrin, and Excedrin P.M. relieve tension and that it lacked a reasonable basis for making those claims. The ALJ found that the claims had been made (F. 247-252, 328-336, 358) and that respondent lacked a reasonable basis for making them. (I.D. 231-232)[71] From these findings, Bristol-Myers has appealed.

First, it is necessary to determine whether respondent represented that the products will relieve tension. Respondent argues that the ads in question claim the products will relieve headache pain and thereby relieve the tension caused by that pain, or that by relieving headache pain they will lessen the tension exacerbated by that pain. (R.A.B. pp. 22-23) However, tension can exist separate from headache pain and we find that respondent has made broader claims about the tension relief characteristics of Bufferin and Excedrin.

In CX 53, respondent represented that Bufferin will relieve tension. The ad depicts a confrontation between a college dean and a student. The tension of the situation is conveyed by a close-up view of the student's clenched fist and by the student's

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71 Complaint paragraph 12 also alleges that respondent lacked a reasonable basis for claims that Excedrin P.M. is an effective mild sedative. This portion of paragraph 12 was dismissed by the ALJ. Complaint Counsel have not appealed the dismissal and we see no reason to reverse the ALJ on this point.

threatening posture. Although part of the audio portion of the ad speaks of headache pain, the visual impression of the ad is that Bufferin should be taken to produce a calming effect after a tense situation.[72] Given the language of this ad, some consumers could infer only that Bufferin relieves headaches caused by tension. However, the copy tests provide strong evidence showing that a substantial number of viewers (54%) received the impression that Bufferin relieves tension and we find that this claim was made by the ad.[73]

Respondent's advertising also represented that Excedrin will relieve tension. This claim is made by those ads which depict Excedrin's chemical formula and state that one of Excedrin's four ingredients is "a tension reliever to relax you."[74] A portion of most of these ads is devoted to Excedrin's ability to relieve headaches. However, in each instance, the depiction of the chemical formula (and the tension relief claim) is separated from the first portion of the ad. Furthermore, these ads stress that Excedrin has four discrete ingredients each of which performs a discrete function. Thus, it is reasonable to conclude these ads make the claim that Excedrin will relieve tension.

The ALJ also found that certain other ads depict headache sufferers in tense situations and thereby imply that Excedrin relieves tension. For example, CX 127 states:

> What is an Excedrin headache? Well, if you suddenly discover a whole pile of unpaid bills . . . . That's a

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72 Similar tense situations are depicted in CX 48, 49, 52, 54-60.

73 Respondent argues that the 54% figure is misleading because test subjects may not distinguish between "free-floating" tension and tension caused by pain. (R.A.B. p. 30) However, the verbatim portion of the copy test makes it clear that a substantial number of viewers received the impression that Bufferin has a calming effect. The ALJ quoted five of these verbatim responses in F. 251. Respondent apparently misinterpreted this finding and concluded that there were only five viewers who believed that Bufferin would relieve tension. In fact, 29 of the verbatim responses relate to Bufferin's ability to relieve tension and appear to distinguish that ability from Bufferin's ability to relieve pain. (See CX 299H-Q.)

74 For example, CX 115, 116, 124, 125, 132, 133, 135-137, 143.

> headache. If four of them are from the electric company . . . [the scene goes dark], that's an Excedrin headache. And for Excedrin headaches, you want Excedrin strength. Excedrin, made stronger against pain and stronger against its tension . . . ."[75]

While this is a close call, we agree with the ALJ that this ad implies that Excedrin will relieve tension. The ad shows, somewhat humorously, a tense situation and then indicates that Excedrin will provide complete relief by relieving both headache and tension. At the close of the ad, the video portion depicts an Excedrin bottle. Superimposed over the bottle are two phrases, "Stronger against pain," and "Stronger against tension." This enhances the impression that Excedrin performs discrete functions, one of which is the relief of tension. Therefore, we find that consumers would reasonably infer that this ad and others like it represent that Excedrin is able to relieve tension. Further support for this is CX 288, a copy test of a similar ad which shows that 23% of the viewers found Excedrin's ability to relieve tension to be a major idea communicated by the ad.

We are unable to agree with the ALJ that respondent represented that Excedrin P.M. will relieve tension. The ALJ found that this representation was made in CX 216 and 219. But the message conveyed by these ads is not that Excedrin P.M. relieves tension; rather it is that the product will relieve the headache pain which causes tension. The ads also represent that Excedrin P.M. has an ingredient "that gently helps you to sleep." However, none of these ads represents that Excedrin P.M. will relieve tension *per se*.

Respondent presented some evidence which it contended constituted a reasonable basis for the tension relief claims. However, the ALJ did not agree with respondent, and we concur. *Pfizer* sets forth several criteria which must be considered in determining whether respondent has a reasonable basis for its tension relief claims. These claims advise consumers to

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75 Examples of other similar ads are CX 128, 135-137, 143.

take aspirin-based analgesics for relief of a specific sympton—tension. If Bufferin and Excedrin are unable to provide tension relief, then consumers may forego effective remedies and are needlessly being encouraged to consume aspirin, a drug with potentially hazardous side effects (see infra p. 53). Furthermore, as with other performance claims related to analgesics, it is virtually impossible for consumers to verify whether or not an analgesic is able to relieve tension. Thus, these considerations should be taken into account in determining the adequacy of respondent's substantiation.

Respondent called no expert witness to support its tension relief claims but instead has relied upon six pieces of evidence, including the results of four studies (none of which were funded by Bristol-Myers (F. 690), and one article and one section from a textbook. The 1957 report on the study by Boyd, Gittinger, and Schimmer does not provide a reasonable basis for respondent's claims because it tested a drug called Effisin which contained no component in common with Bufferin and contained only salicylamide in common with Excedrin. Respondent never claimed any tension relieving properties for salicylamide. (Lanman, Tr. 11509-10, 12149-51.) The 1959 report by Boyd, *et al.* was reviewed by Dr. Rickels, complaint counsel's expert on pharmacology and tension, and he pointed out that the authors tested subjects who had pain (not just tension) and the study's results might be attributable to the pain relieving properties of aspirin. (Rickels, Tr. 6593) He also stated that he had "great doubts about the results" of the study because they showed Bufferin's tension relieving abilities as exceeding those of most prescription drugs prescribed for tension relief. (Rickels, Tr. 6591-95) Two studies reported in 1964 and 1965 by Krumholtz and Merlis also do not constitute a reasonable basis because the authors recognized the data's deficiencies. (Lanman, Tr. 12258) Furthermore, Dr. Rickles noted that these studies were not randomized and had numerous other flaws. (Rickels, Tr. 6572-80)

Respondent also submitted a 1954 textbook and a 1957 review article. Neither was based on clinical trials. Dr. Rickels noted that the FDA Panel on OTC Sedatives, Tranquilizers

and Sleep-Aid Drug Products (which he chaired for three years) did not consider such textbooks and articles as evidence of a drug's efficacy. (Rickels, Tr. 6547-48) In 1965, when all evidence submitted by respondent was extant, Dr. Beaver, an expert in the field of analgesics and the clinical testing of analgesics (F. 20), conducted a review of all evidence—including evidence solicited directly from Bristol-Myers—on the pharmacological properties of analgesics. (Beaver, Tr. 5897-5900) As a result of his review (which specifically considered the 1964 and 1965 studies by Krumholtz and Merlis), Dr. Beaver concluded that there was "no good evidence" that mild analgesics have tension relieving properties. (Beaver, Tr. 5897-98; Lanman, Tr. 12151-54) The adequacy of respondent's evidence has been subsequently cast into further doubt by a well-controlled 1973 study which showed that aspirin was not significantly different from a placebo in its ability to relieve tension (Rickels, Tr. 6500, 6511-14, 6517) and by the FDA OTC Analgesics Panel which concluded that aspirin is "clearly ineffective" for "nervous tension." (CX 514, p. 35353) Thus, in light of the kind of claims made by respondent (and their pontential impact), the limited relevance of evidence submitted by respondent and the expert testimony, we find that respondent did not possess a reasonable basis for claims that Excedrin and Bufferin relieve tension.[76]

IV The Doctors Recommend Claim

Paragraphs 17 and 18 of the complaint allege, and the ALJ found, that respondent's ads represent that physicians recommend Bufferin more than any other nonprescription internal analgesic and that there is no reasonable basis for the claim. Respondent does not contest that it lacks a reasonable basis for the claim that physicians recommend Bufferin more than any

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76 Indeed, Excedrin contains caffeine, a substance which is contraindicated for the relief of tension (Rickels, Tr. 6530-31) and which is described as "nerve-jangling" and "sleep-disturbing" in a 1968 ad for Bufferin. (CX 106)

OTC analgesic.[77] However, it argues that the ads represent only that physicians recommend Bufferin more than any other *leading brand* of OTC analgesic and that the evidence it has presented constitutes a reasonable basis for that claim. Thus, we must determine what is represented by the ads in question.

We find that in numerous ads respondent has represented that doctors recommend Bufferin more than any other OTC analgesic. For example, in CX 3, the video portion states, "Doctors specify Bufferin most." At the same time the announcer states, "Of all leading brands of pain reliever you can buy for minor pain, doctors specify Bufferin most."[78] Although the literal message contained in the audio portion is that Bufferin is specified more frequently than leading *brands*, consumers could reasonably infer that Bufferin is recommended more frequently than all other OTC analgesics. (Certainly consumers cannot be expected to realize that the product doctors recommend most, aspirin, is not a brand.) This is also the message in the video portion. We believe the open-ended statement, "Doctors specify Bufferin most" would reasonably be interpreted to mean that doctors specify Bufferin more than any other OTC analgesic and the audio portion might not override that impression.[79]

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77 Respondent submitted portions of two surveys in support of the "doctors recommend" claim. (CX 364-390) These data do show that from 1967 through 1971 doctors recommended Bufferin more than Bayer, Excedrin and Anacin. (See CX 838J-R) However, these data also show that for pain relief, doctors recommend Tylenol, Ascriptin and generic aspirin more often than Bufferin. (See CX 822Y-Z)

78 Similar ads are CX 2, 4-7, 41-46, 65-67, 97, 107.

79 Respondent argues that the copy test of CX 3 does not show that a substantial number of consumers received the impression that doctors recommend Bufferin more than any other OTC analgesic. (CX 301) However, as we indicated above (supra p. 12), although a copy test may verify the primary theme of an ad, it is less likely to demonstrate the presence of secondary themes. Since the ad makes several claims (including speed, efficacy, less stomach upset, long-lasting relief) in addition to the "doctors recommend" claim, the copy test might well not accurately measure the extent to which consumers received a particular message from an ad which contained a number of messages.

Thus, we find that respondent's ads represent that doctors recommend Bufferin more than any other OTC analgesic, and that respondent lacked a reasonable basis for making that claim.

V REPRESENTATION THAT BUFFERIN AND EXCEDRIN CONTAIN OTHER THAN ORDINARY ASPIRIN; FAILURE TO DISCLOSE THE PRESENCE OF ASPIRIN

Paragraph 21 of the complaint charges respondent with representing that the analgesic ingredient in Bufferin is other than ordinary aspirin, that the ingredient in Excedrin which provides long-lasting relief is other than ordinary aspirin, and that the antidepressant in Excedrin is other than caffeine. Paragraph 19 charges that respondent failed to disclose that Bufferin, Excedrin, and Excedrin P.M. contain aspirin and that Excedrin contains caffeine.

Respondent argues that its ads do not indicate that its products contain an analgesic other than aspirin. It claims that the ads for Bufferin contrast the total product of Bufferin with aspirin. It further claims that Excedrin ads compare its ingredients to aspirin but in no way imply that Excedrin does not contain aspirin. Finally, respondent argues that the presence of aspirin in Bufferin and Excedrin is not material to consumers and that the ALJ's order requiring disclosure of aspirin is improper. Specifically, it argues that aspirin is harmful to only a small group of consumers and these consumers already know that Bufferin and Excedrin contain aspirin.

We disagree with respondent and find that its ads do represent that Bufferin and Excedrin contain other than ordinary aspirin. All three products, Bufferin, Excedrin, and Excedrin P.M., contain aspirin and no ad for any of them discloses that fact.[80] In addition, numerous ads for Bufferin attempt to

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80 The active ingredients of one tablet of each of the three preparations are:

Bufferin:	aspirin	5 grains
	magnesium carbonate	97.2 mgs.
	aluminum glycinate	49 mgs.

differentiate its analgesic ingredient from aspirin. This is accomplished by several means. First, through the use of strained syntax, ads make it appear that Bufferin contains something other than aspirin. For example, CX 7 states:

> In the first 30 minutes Bufferin delivers twice as much pure pain reliever as the best known aspirin.

This ad compares Bufferin's analgesic ingredient, and not its total formula, with aspirin. In no ad for Bufferin is its analgesic ingredient referred to as aspirin. Instead, it is called "pain reliever" (CX 33), "pure pain reliever" (CX 13), "active pain reliever" (CX 27), "high-speed formula" (CX 34), and "strong medicine" (CX 52). These characterizations, in and of themselves, would not necessarily lead to deception. However, in each of these ads aspirin is specifically mentioned and is carefully differentiated from Bufferin. In addition, ads create the impression that Bufferin is different from aspirin by contrasting Bufferin's analgesic performance with aspirin. For example, CX 39 states:

> What a time for a headache. You could have taken aspirin . . . but Bufferin goes to work in half the time of simple aspirin. Look. Simple aspirin takes 20 minutes to give you the pain reliever Bufferin gives you in 10.

As another example, CX 50 states, "Plain aspirin's fine, but Bufferin goes to work much faster." Always Bufferin is distinguished from aspirin. By virtue of the wording of these ads, consumers would reasonably infer that the analgesic in Bufferin is other than ordinary aspirin.

Excedrin:	aspirin	3 grains
	acetaminophen	1.5 grains
	salicylamide	2 grains
	caffeine	1 grain
Excedrin P.M.:	aspirin	3 grains
	acetaminophen	2.5 grains
	salicylamide	2 grains
	methapyrilene furmarate	25 mgs.

Although no ad for Excedrin discloses that it contains aspirin, several ads affirmatively disguise that fact. For example, CX 115 contains a graphic representation of the chemical formulas of Excedrin and one of its competitors. The ad first depicts the competitor's formula and identifies its ingredients as aspirin and caffeine. Below that, Excedrin's formula is displayed. However, Excedrin's ingredients are not identified. They are merely referred to as "four medically endorsed ingredients" providing "quick relief, long-lasting relief, a tension reliever to relax you, an antidepressant to restore your spirits." The second ingredient, the one providing "long-lasting relief" is, in fact, aspirin. Its formula is placed below caffeine in the competitor's formula. Thus, a viewer may be unlikely to realize that aspirin is contained in Excedrin. Indeed, by virtue of the juxtaposition of ingredients, it appears that Excedrin does not contain aspirin. The same technique is used to disguise the presence of caffeine. Caffeine is referred to as "an antidepressant to restore your spirits." Its formula is not placed below caffeine in the competitor's product and consumers could be led to believe that Excedrin contains no caffeine.[81]

CX 141 creates the impression that Excedrin does not contain aspirin by stressing the aspirin content of its competitors. It states:

> This pain reliever says it works wonders. And it does. It's plain aspirin. This pain reliever says it has more of the ingredient doctors recommend most. And it does. They mean plain aspirin. [Excedrin] says it's the extra strength pain reliever and it is. Excedrin's four ingredient formula gives you quick relief, long lasting relief, a tension reliever to relax you. An antidepressant to help restore your spirits.

The failure to disclose the presence of aspirin in Excedrin in the context of this ad makes it appear that Excedrin does not contain aspirin.

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81 CX 116 is similar.

Thus, we find that consumers could reasonably infer from the ads discussed above that Bufferin and Excedrin do not contain ordinary aspirin.[82] Our analysis of these ads is similar to that in *American Home Products,* 98 F.T.C. at 365-367, and, as in that decision, we conclude that the representations in these ads had the capacity to mislead consumers. Nevertheless, a misleading claim or omission violates the FTC Act only if the omitted information would be a material factor in the consumer's decision to purchase the product. *F.T.C.* v. *Colgate-Palmolive Co.,* 380 U.S. at 392. "Materiality" is defined in Section 15 of the FTC Act, 15 U.S.C. § 55, the section which defines "false advertisement."[83] It provides that an omission of fact may be material "in the light of representations made or suggested . . . or . . . with respect to consequences which may result from the use" of the product.

In light of the "representations made or suggested" in the advertisements discussed above, there can be little doubt that the presence of aspirin in Bufferin and Excedrin is material to consumers. Indeed, the fact that ads for Excedrin and Bufferin carefully differentiate their formulas from aspirin and then use

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82 However, we find that some of the Excedrin ads cited by the ALJ do not disguise the presence of aspirin. For example, CX 132 makes no comparison between Excedrin and aspirin. Aspirin is never mentioned in the ad and Excedrin's ingredients are not described as special or different. Thus, although this ad and others like it (e.g. CX 122-131, 133, 134, 136-139, 142-152) do not disclose the presence of aspirin, we do not believe that they create the misimpression that Excedrin does not contain aspirin.

Respondent argues that there has been no showing that the aspirin contained in Bufferin and Excedrin is "ordinary." (R.A.B. pp. 37, 38; Bristol-Myers Reply Brief pp. VIII-1–VIII-2.) However, complaint paragraph 21 alleges that respondent misled consumers by creating the impression that Bufferin and Excedrin did not contain aspirin, a common, well-known analgesic. Thus, as used in paragraph 21, the word "ordinary" refers to the fact that aspirin is well-known. It does not refer to the quality of the particular type of aspirin used in Bufferin and Excedrin.

83 The definition of "false advertisement" in Section 15 applies to that term as it is used in Section 12. Since respondent is charged with violating both Sections 5 and 12, the definition in Section 15 is directly relevant to the case.

these apparently special formulas as principal selling messages strongly implies that knowledge of the presence of aspirin would be material to consumers. Furthermore, the presence of aspirin in Bufferin and Excedrin is made all the more significant by virtue of aspirin's potential side effects. As we found in *American Home Products*, 98 F.T.C. at 368-369, and as was testified to in this case by Dr. Grossman and Dr. Donald Stevenson (an immunologist who is an expert in the area of asthma and allergy), aspirin may have numerous side effects. It may cause dyspepsia and gastrointestinal bleeding and it may exacerbate or even cause ulcers. (Grossman, Tr. 7724-28, 7741-45, 7821, 7985) Aspirin can cause asthmatics to suffer attacks which may be severe or even life threatening. (Stevenson, Tr. 1480, 1489) It can also cause skin reactions such as hives and swelling. (Stevenson, Tr. 1512)

Although respondent recognizes that these side effects may occur, it argues that since only a very small percentage of users actually suffer these side effects, the disclosure of aspirin's presence is not material. Nevertheless, as we found in *American Home Products,* 98 F.T.C. at 367, the actual number of individuals who may be adversely affected is significant. Furthermore, the disclosure of aspirin's presence is material not only to individuals who actually suffer adverse effects but also to those who *may* suffer effects. For example, immunologists generally warn all asthmatics to avoid aspirin (Farr, Tr. 2601, 2606), and some studies indicate that more than 10% of the population suffers from asthma. (Stevenson, Tr. 1498; Farr, Tr. 2589-2605) For this portion of the population, the presence of aspirin is material.

Respondent next argues that disclosing the presence of aspirin in ads for Bufferin and Excedrin is unnecessary because consumers who may be allergic to aspirin (such as asthmatics) have been warned by their physicians to avoid aspirin and to read labels. The labels for Bufferin, Excedrin, and Excedrin P.M. do disclose the products' aspirin content. (R.A.B. p. 42, 44)[84] However, the nondisclosure of aspirin is material in light

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84 The ALJ found that studies show a substantial number (in excess of 60%) of consumers do not know that Bufferin and Excedrin contain aspirin.

of both "the consequences which may result" from aspirin's use and respondent's representations regarding aspirin.[85] As discussed above, numerous ads for Bufferin and Excedrin create the impression that those products do not contain aspirin. Consumers receiving that impression might feel no need to examine the label. The importance of this misleading initial contact is recognized in *Carter Products, Inc.* v. *F.T.C.*, 186 F.2d 821 (7th Cir. 1951), which held that when the first contact between a seller and a buyer occurs through a deceptive advertisement, the law is violated even if the truth is subsequently made known to the purchaser through information on the label. In this case, of course, we have no assurance that consumers do actually read labels. And, even if consumers do subsequently read the label, they may have already purchased the product unnecessarily, thereby causing themselves economic harm.

Respondent argues that the legislative history of the FTC Act precludes finding the nondisclosure of aspirin to be material. Specifically, it cites a portion of the conference report regarding Section 14 of the Act, 15 U.S.C. § 54, which states that criminal sanctions are not to be imposed for false advertising if the commodity which is falsely advertised is injurious to

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(F. 673-679) This conclusion was based upon numerous consumer surveys in the record including CX 314, 333, 347, 348, 810, 1058, and 1059. The record also contained (and the ALJ relied upon) an analysis of these surveys by Dr. Ivan Ross, the complaint counsel's expert in marketing research, and he concluded that "a substantial number of people are not aware that aspirin is an ingredient of either Bufferin or Excedrin." (Ross, Tr. 7456) Respondent disputes the methodology of four of the surveys relied on by the ALJ (R.A.B. p. 43 n*) but does not question the other three. Furthermore, respondent has offered no expert testimony to dispute the ALJ's finding. Thus, we believe the ALJ correctly concluded that evidence shows a substantial number of consumers do not know that Bufferin and Excedrin contain aspirin.

85 Despite aspirin's harmful side effects, we are unprepared to hold that the mere failure to disclose the presence of aspirin in advertising for aspirin-based analgesics renders that advertising materially misleading. Respondent's affirmative misrepresentations (both express and implied) that Bufferin and Excedrin *do not* contain aspirin are essential elements to our finding of liability.

consumers' health only because of peculiar idiosyncracies or allergic conditions. (R.A.B. p. 38)[86] It argues that this section of legislative history also applies to Section 15 because Sections 14 and 15 share some wording in common.[87] However, respondent's argument regarding Section 15 is inappropriate for two reasons. First, we have found respondent's advertisements misleading not merely because of the nondisclosure of aspirin, but because of the combined effect of affirmative statements implying that the products do not contain aspirin *and* the failure to disclose aspirin. Both elements, affirmative statements and nondisclosure, are essential to our finding of materiality in this case. Indeed, in the order we enter today, we do not require respondent to disclose the presence of aspirin in every ad for Bufferin and Excedrin, only in those ads which contrast the product's ingredients with an aspirin-containing product. Second, arguments regarding Section 14 (such as the one made by respondent) do not necessarily apply by analogy to Section 15. Section 14 imposes criminal sanctions and Section 15 does not. That fact alone is reason for applying a different standard under Section 15. There is also no reason to believe that Congress intended to restrict the definition of misleading advertisements in the same way it restricted the imposition of criminal sanctions. The legislative history of Section 14 quoted by respondents refers to penalization and there is no similar language in the legislative history interpreting Section 15.

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86 House of Representatives Report No. 1774, February 8, 1938. Conference Report, page 10.

87 Section 14 states that criminal sanctions may be imposed if:

> . . . the use of the commodity may be injurious to health because of results of such use *under the conditions prescribed in the advertisement thereof or under such conditions as are customary or usual* . . . .

Section 15 states that in determining whether an ad is misleading in a material respect, the Commission must take into account:

> . . . consequences which may result from the use of the commodity to which the advertisement relates *under the conditions prescribed in said advertisement, or under such conditions as are customary or usual.*

The section of the conference report cited by respondents comments on the underlined portion of Section 14.

Respondent also argues that by virtue of dissimilarities between Section 15 of the FTC Act and portions of the Food, Drug, and Cosmetics Act, its advertisements should not be found to be false advertisements as that term is defined in Section 15. Bristol-Myers points out that the same Congress which enacted Section 15 also enacted amendments to the FDCA which apply to misbranded drugs. These amendments state that a drug is misbranded if its label does not disclose its ingredients. 21 U.S.C. § 352(e)(ii). Respondent argues that since Section 15 does not mention disclosure of ingredients, Congress did not intend that failure to disclose ingredients would constitute false advertising. It is true that Section 15 does not say that every ad which fails to disclose ingredients violates the law. But, once again, we have found respondent's ads misleading because of affirmative statements *and* nondisclosure. This is not a case of simple nondisclosure; therefore, respondent's argument is not germane.[88]

VI Claim That Excedrin P.M. Contains A Special Ingredient

Complaint paragraphs 23 and 24 allege, and the ALJ found, that respondent has falsely advertised that Excedrin P.M. contains a special sedative or sleep-inducing agent available only in Excedrin P.M. when in fact the ingredient, methapyrilene fumarate, is available in several other OTC drugs. We disagree with the ALJ's finding and conclude that this representation was not made by respondent's advertising.

According to the ALJ, numerous ads represent that Excedrin P.M.'s sleep-inducing ingredient is unique. (F. 359) However, we find that, at most, these ads represent that the formulation of Excedrin P.M. is unique. For example, CX 218 states, in its entirety:

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88 The ALJ determined that the record in this case did not show that the presence of caffeine in Excedrin is a material fact which should be disclosed in ads. (I.D. 243-244) Complaint counsel did not appeal this point and we see no reason to reverse the ALJ's decision.

> There's a new idea for bedtime headaches. It's more than a pain tablet but it's not a strong sleeping pill. It's new Excedrin P.M., the night-time pain reliever. It combines pain relief with a special night-time ingredient that gently helps you sleep. Excedrin P.M. is a new idea. Excedrin P.M., the night-time pain reliever.

The message in this ad is that Excedrin P.M. is new and different, not that the sleep-inducing ingredient is unique. Although that ingredient is referred to as "special," in the context of this ad, that appears to suggest that the ingredient has a special purpose, a purpose other than pain relief. After considering all the ads cited by the ALJ, it is our conclusion that in no instance do those ads represent that the sleep-inducing ingredient is unique. Thus, we dismiss the allegations of complaint paragraphs 23 and 24.[89]

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89 In addition to substantive objections discussed in Sections II-VI above, Bristol-Myers objects to numerous evidentiary rulings by the ALJ. (R.A.B. pp. 18-20, 75-77) First, it contends that certain medical documents (CX 510, 511, 512, 514, 518) should not have been admitted into evidence because it was not given an opportunity to depose the authors or probe into underlying data. It is not necessary for us to resolve this issue because we do not believe that any error which may have occurred regarding these documents substantially prejudiced respondent's rights. No portion of our decision is based on these documents. Indeed, our decision makes no reference to CX 510, and the few references we have made to the other documents are only to provide additional support for propositions which are adequately supported by expert testimony on the record. Similarly, we do not believe that the inclusion of documents contradicting the testimony of Dr. Azarnoff prejudiced respondent since each reference to his testimony is accompanied by a reference to at least one other expert witness.

Bristol-Myers also objects to the ALJ's refusal to accept into evidence a study on Excedrin performed by Dr. Sunshine. The ALJ excluded this study because it was not listed by Bristol-Myers on its pre-trial document list. (Tr. 9626-9635) We decline to overturn the ALJ's decision on this point because it was an appropriate exercise of the ALJ's duty to manage fairly and efficiently the progress of a complex lawsuit. Without full pre-trial disclosures, it would be impossible to conduct an orderly trial in a case such as this one. Furthermore, this rejected study was one of a group of studies rejected by the ALJ. Bristol-Myers was subsequently given the opportunity to introduce one of the studies but chose not to do so unless all would be

VII ADVERTISING AGENCIES' LIABILITIES

The ALJ concluded that Ted Bates & Company, Inc. and Young & Rubicam, Inc., two advertising agencies employed by Bristol-Myers, were also liable for certain of the advertising claims regarding Bufferin, Excedrin, and Excedrin P.M. We concur with certain parts of the ALJ's decision but have modified the order to reflect our areas of disagreement.

In order to hold an advertising agency liable for false advertising, the agency must have been an active participant in preparing the violative advertisements, *Doherty, Clifford, Steers & Shenfield, Inc.* v. *F.T.C.*, 392 F.2d 921, 927 (6th Cir. 1968); *American Home Products*, 98 F.T.C. at 396, and it must have known or had reason to know that the advertisements were false or deceptive. *Doherty*, 392 F.2d at 927; *Standard Oil Co.*, 84 F.T.C. at 1475. It is undisputed in this case that the advertising agencies actively participated in the preparation and dissemination of certain of the challenged ads in this proceeding. Furthermore, an advertising agency is held to know the claims made in the advertisements which it has prepared. *In re Merck & Co.*, 69 F.T.C. 526, 559 (1966), *aff'd*, 392 F.2d 921 (6th Cir. 1968). Thus, what remains to be determined is whether the agencies knew, or had reason to know, that the ads in question were false or deceptive due to the failure to disclose material facts, the lack of a reasonable basis, or the lack of scientific establishment.

In determining whether an advertising agency knew or had reason to know that an ad was false or deceptive, it is

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accepted into evidence. Apparently respondent believed that it was the pooled results of all the studies which supported Excedrin's superiority. (Tr. 11616-18) Nonetheless, the ALJ did permit respondent's experts to refer to the pooled results. In addition, the record shows that none of these studies was among the evidence submitted by Bristol-Myers to either the FDA OTC Analgesics Panel or the *AMA Drug Evaluations* to support claims of Excedrin's extra strength. (Lanman, Tr. 12116-17; Sunshine, Tr. 9702-06) Thus, we are not able to conclude that the ALJ abused its discretion in excluding these studies. Similarly, we think that the ALJ correctly refused to accept into evidence those portions of the new drug application for Extra Strength Tylenol and certain additional blood level data regarding Bufferin submitted by respondent.

necessary to examine carefully the claim made in the challenged ad and the type of substantiation necessary to support the claim. Surely, an advertising agency cannot be required to conduct an independent investigation to determine whether a scientific claim has been established. However, with respect to certain claims, it may be that the disparity between the claims and the substantiation is so great as to preclude a conclusion that the ads in question were conceived through reasonable reliance on the substantiation provided by the manufacturer of the product. *Standard Oil Co. of California*, 84 F.T.C. at 1474-75.

A. Ted Bates & Company, Inc.

Respondent Ted Bates & Company, Inc., (Bates) actively participated in the creation and dissemination of advertisements for Bufferin beginning in 1968. Thus, Bates was responsible for making the same claims regarding Bufferin which we found were made by respondent Bristol-Myers. Bates has not denied that it participated in the creation and dissemination of any of the ads listed in F. 797 and CX 800. But it has appealed the ALJ's conclusion that the ads make the challenged representations. (Ted Bates Appeal Brief pp. 7-10, 12-16, 17-19) However, we find no reason to alter any of the conclusions which we reached above regarding the Bufferin advertisements and we find that Bates is responsible for the ads which make false or deceptive claims regarding Bufferin.

The ALJ determined that with respect to the claims of Bufferin's established superior efficacy, respondent Bates reasonably relied on the substantiation provided by Bristol-Myers and was, therefore, not liable for the fact that those claims had not been established. From this determination, complaint counsel have appealed. Complaint counsel contend that documents from Bates' files (e.g. CX 469B, 556) demonstrate that Bates knew the establishment claims were open to substantial question. (CAB p. 54) They point out that Bates was not required to perform any analysis of the support presented by Bristol-Myers since the documents in their files should have demonstrated the falsity of the claims they were making.

Therefore, complaint counsel contend that Bates' reliance on the substantiation provided by Bristol-Myers was not reasonable.

We are unable to agree with complaint counsel on this point. Although we found that the comparative efficacy claims regarding Bufferin had not been established, there definitely was some evidence supporting Bufferin's claims of superior speed (*see* e.g., F. 592, 606-607) and superior freedom from side effects (F. 634). This evidence provided at least some facial support for the claims but did not establish them. A major drug company, such as Bristol-Myers, may be expected to perform the sort of analysis necessary to determine whether a claim has been established; an advertising agency is far less capable of performing such a task. That task is a complicated one (as demonstrated by Section II of this opinion) requiring both scientific and statistical expertise and demanding familiarity with work done by other experts in the field. We are unwilling to require that Bates perform this sort of examination of the universe of knowledge related to analgesics.

It is true that some documents in Bates' files do question Bufferin's superiority. However, this fact alone would not preclude a finding that Bates reasonably believed that the claims had been established since we have found that Bates possessed other evidence which provided some scientific basis for the claims that were made in the ads. We concluded from the expert testimony and other evidence in this case that in order to establish the comparative claims made for Bufferin, scientists generally would require two well-controlled clinical tests. But even if a claim has been established, that does not mean that the claim is unanimously regarded as correct. There will always be disagreements and documents reflecting that disagreement. While we might expect an advertiser to determine whether conflicting opinions would negate a finding that a claim had been established, we would not require an advertising agency to perform the same level of analysis. We thus find that the documents in Bates' files do not render Bates liable for the lack of support for the establishment claims.

This decision is not inconsistent with out past decisions finding ad agencies liable for inadequately substantiated advertising. In *Merck & Co., Inc.*, 69 F.T.C., 526, 558-559 (1966), *aff'd sub nom. Doherty, Clifford, Steers and Shenfield, Inc.* v. *F.T.C.*, 392 F.2d 921 (6th Cir. 1968), we found an advertising agency liable for deceptive ads because it developed an advertising campaign which went far beyond the substantiation provided by the drug company. In *ITT Continental Baking Co.*, 83 F.T.C. 865, 968-969 (1973) *order modified in part*, 532 F.2d 207 (2d Cir. 1976), we held an advertising agency (by coincidence, Ted Bates & Co., Inc.) liable for false advertising claims which lacked any substantiation. The agency argued that it had no reason to know that the claim was deceptive. In response to this, we affirmed that an agency does have a duty to ascertain the existence of substantiation for the claims which it makes. However, as we also stated, "No issue is raised in the instant case of agency reliance on the accuracy of a scientific test conducted by third parties." *Id.* at 969. Once again, in *Standard Oil Company of California*, 84 F.T.C. 1401, *order modified* 577 F.2d 653 (9th Cir. 1978), we found an advertising agency liable because its advertised claims "went far beyond even the most favorable interpretation of test results or other research data available when the advertisements were created and distributed." *Id.* at 1474. Finally, in *American Home Products*, 98 F.T.C. at 309, we held that "when presented with a facially inadequate study as substantiation, an advertising agency may not ignore the study's defects."

In this case (unlike any of the above-cited cases), the substantiation possessed by respondent Bates did tend to support the claims in the Bufferin advertisements and the studies were not facially inadequate. We found Bristol-Myers liable because it did not possess substantiation of the type and quantity necessary to establish the claims it made. We do not intend to require an advertising agency to perform the inquiry necessary to determine what level of substantiation relevant experts require to establish a comparative claim regarding OTC drugs. Thus, we find that complaint counsel failed to show that the evidence in the record was sufficient to put Bates on notice that

adequate substantiation was lacking and respondent Bates is not liable for the violations charged in paragraphs 7 and 8 of the complaint.

Respondent Bates appeals from paragraph IV A of the ALJ's order which would prohibit it from representing that Bufferin will not upset a person's stomach unless it possesses a reasonable basis for making that claim. Bates argues that the order provision was improper because the complaint raised no issue as to the reasonableness of the "no stomach upset" claim. (Ted Bates Appeal Brief p. 10) This is true (*see* Tr. 11613-14), and we find that paragraph IV A of the ALJ's order is inappropriate.

Bates next objects to paragraph IV B of the ALJ's order, which prohibits it from representing without a reasonable basis that Bufferin will relieve tension. Bates argues that since the ALJ found that Bates had a reasonable basis for the tension-relief claim (I.D. 256), entry of the order provision was improper. Complaint counsel do not oppose deletion of this provision. (C.R.A.B. p. 55) As the ALJ observed in discussing the issue of Bates' liability:

> what may not be a reasonable basis for a medical-scientific claim for a drug manufacturer may be a reasonable basis for an advertising agency which relied in good faith on the client drug manufacturer's judgment regarding the adequacy of substantiation unless the purported substantiation was unreliable on its face. (I.D. 256)

We find that the substantiation for the tension relief claim did constitute a reasonable basis for Bates (although not for Bristol-Myers). Since Bates did not violate the FTC Act with respect to the claims of tension relief, paragraph IV B of the ALJ's order is inappropriate. *ITT Continential Baking Co., Inc.* v. *F.T.C.*, 532 F.2d 207, 221 (2d Cir. 1976).

Respondent Bates also objects to paragraphs IV C and D of the ALJ's order. These provisions would prohibit Bates from referring to aspirin by any name other than aspirin and would require it to disclose in advertisements that Bufferin contains aspirin. Bates contends: (1) that the ads do not imply that

Bufferin contains something other than aspirin, and (2) that even if they do, Bates neither knew nor had reason to know that the presence of aspirin in Bufferin is a material fact.

First, as we explained above, a substantial number of ads for Bufferin do imply that Bufferin does not contain aspirin and that its formula is somehow special (*supra* pp. 50-51). Second, we find that Bates had reason to know that the presence of aspirin in Bufferin was a material fact.[90] Bates developed numerous ads which create the impression that Bufferin does not contain aspirin. This false inference was central to these ads, and these ads were central to the advertising campaign for Bufferin. From this we infer that Bates knew (or at least should have known) that knowledge of the presence of aspirin in Bufferin would be material to consumers and that it was, therefore, important to disguise that fact and even to create the impression that aspirin was not a component of Bufferin. Thus, we find that respondent has committed the violations alleged in paragraphs 19-22 of the complaint.

Finally, respondent Bates objects to paragraph IV E of the ALJ's order. (Ted Bates Appeal Brief pp. 21-22) This provision would prohibit Bates from representing that doctors recommend Bufferin more than any other OTC analgesic unless Bates has a reasonable basis for making the claim. First, Bates argues that it did not develop the "doctors recommend" campaign. That may be so. However, Bates clearly participated actively in the preparation of ads making the claim even if the claim was initially developed by another advertising agency. To hold Bates liable for the claim, it is not necessary to establish

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90 Bates argues that paragraphs IV C and D of the ALJ's order are inappropriate because it has not been shown that (1) Bates knew that consumers were unaware of the presence of aspirin in Bufferin; and (2) Bates knew that aspirin might be injurious to health. (Ted Bates Appeal Brief, p. 19) However, it is not necessary for complaint counsel to demonstrate either of these propositions. We have already determined that the presence of aspirin in Bufferin is a material fact by virtue of the health hazards associated with aspirin and the misleading claims that were made for the product (supra p. 53). To find the advertising agency that developed the ads liable, all that remains to be determined is whether it knew or had reason to know of that materiality.

that it was the original developer of the campaign. Second, Bates argues that the ads only represent that doctors recommend Bufferin more than other leading brands. However, as we explained above (*supra* pp. 48-49) consumers could reasonably infer from the ads in question that Bufferin is recommended more frequently than all other OTC analgesics. Bates' third argument is that no ad made the "doctors recommend" claim after 1971 and it would be inappropriate to enter an order provision related to a campaign long discontinued. The mere fact that an unlawful practice has been discontinued does not bar the entry of a cease and desist order. *Fedders Corp.* v. *F.T.C.*, 529 F.2d 1398, 1403 (2d Cir. 1976), *cert. denied*, 429 U.S. 818 (1976). Indeed, abandonment will not constitute a defense to an order provision unless it was done voluntarily and the record contains assurance that the practice will not be resumed. *Rubbermaid, Inc.* v. *F.T.C.*, 575 F.2d 1169, 1172 (6th Cir. 1978). Since the record in this case contains no assurance that the circumstances under which the ad claims were dropped provide a basis for inferring that the "doctors recommend" claim will not be resumed in the future, we have entered an order provision similar to paragraph IV E of the ALJ's initial order.

B. Young & Rubicam, Inc.

Respondent Young & Rubicam, Inc. has actively participated in the creation of advertisements for Excedrin and Excedrin P.M. since prior to 1962. Thus, Young & Rubicam was responsible for making the same claims regarding Excedrin and Excedrin P.M. which we found were made by respondent Bristol-Myers. Young & Rubicam has not denied that it was an active participant in the creation and dissemination of the advertisements for Excedrin and Excedrin P.M. It does contest whether some of the ads make the challenged representations. (Young & Rubicam Appeal Brief pp. 11-12) However, once again, we find no reason to alter our interpretation of any of the Excedrin or Excedrin P.M. ads.

As he did with respect to Bates, the ALJ determined that Young & Rubicam reasonably relied on substantiation pro-

vided by Bristol-Myers supporting the comparative efficacy claims regarding Excedrin and Excedrin P.M. (I.D. p. 256). Complaint counsel have appealed this finding. They contend that prior to Young & Rubicam's receipt of the results of the Emich study in 1970, Young & Rubicam knew that its claims of superior efficacy for Excedrin lacked adequate support. (CAB p. 60) They cite two documents obtained from Young & Rubicam's files which they contend demonstrate Young & Rubicam's knowledge that the pre-1970 claims were false. (CX 469, 628) Thus, they have requested that the ALJ's order against Young & Rubicam be amended to prevent such unsubstantiated comparative efficacy claims in the future.

We decline to amend the order in this fashion. First, as we indicated above in connection with the discussion of the liability of Ted Bates, Inc. (*supra* pp. 60-61), we are unwilling to require an advertising agency to perform independently the inquiry necessary to determine the level of substantiation required by experts to establish a claim of superiority regarding an OTC drug. Furthermore, we agree with the ALJ that "it was not unreasonable for Young & Rubicam to have accepted the [Emich] study at face value and relied on it as reasonable substantiation for the efficacy claims for Excedrin." (F. 812) We also find that prior to 1970, Young & Rubicam possessed the Sherman study (*see supra* pp. 32-33) which is evidence, albeit not clinical evidence, that tended to show that Excedrin was superior to aspirin. Although we agree with the ALJ that CX 496[91] is of questionable materiality in this case (Tr. 3956), we believe that in conjunction with CX 628[92] it raises the question of whether Young & Rubicam knew its claims were inadequately substantiated. However, as we noted before, the mere fact that questions have been raised to an advertising

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91 CX 496 is an unsigned review of a January 1970 Excedrin research and development meeting which casts doubts on Excedrin's superior efficacy. It was obtained by complaint counsel from Young & Rubicam's files.

92 CX 628 is a copy of a letter dated December 1970 from Young & Rubicam to Bristol-Myers which appears to state that the Emich Study represents the first evidence of Excedrin's superior efficacy.

agency regarding advertising claims does not automatically establish that the agency should have known the claims were not adequately substantiated. In this instance, Young & Rubicam possessed some substantiation for the comparative performance claims prior to 1970. Moreover, the evidence shows that only two ads prior to 1970 represented that Excedrin's superiority had been established, and that subsequent to early 1970 the Emich Study constituted adequate facial support for the comparative claims made by Young & Rubicam. In light of these facts, we decline to enter any order provision against respondent relating to comparative performance claims for Excedrin.

Young & Rubicam has raised three issues on appeal. First, it argues that paragraph V D of the ALJ's order is inappropriate. (Young & Rubicam Appeal Brief pp. 5-7) This paragraph would prohibit Young & Rubicam from representing that doctors recommend Excedrin or Excedrin P.M. unless they possess a reasonable basis for making the claim. Young & Rubicam contends that this paragraph should be removed from the order because no such claim was ever made regarding either Excedrin or Excedrin P.M. and Young & Rubicam was never charged with making such a claim. Our examination of the advertisements in evidence in this case shows that no "doctors recommend" claim was ever made regarding either Excedrin or Excedrin P.M. Since the prohibitions in a remedial order must bear a reasonable relation to the respondent's conduct, *Jay Norris, Inc.* v. *F.T.C.*, 598 F.2d 1244, 1249 (2d Cir. 1979), *cert. denied*, 444 U.S. 980 (1979), we agree that paragraph V D of the order is inappropriate.

Young & Rubicam next argues that paragraph V A is inappropriate. (Young & Rubicam Appeal Brief pp. 8-9) This provision would prohibit respondent from representing that either Excedrin or Excedrin P.M. will relieve tension unless Young & Rubicam possesses a reasonable basis for such a claim. Respondent argues that since the ALJ found that Young & Rubicam did possess a reasonable basis for the tension relief claims which it made (I.D. 256), the order provision is inappropriate. The facts regarding this order provision are identical to the facts regarding order paragraph IV B discussed above

(*supra* pp. 61-62) and for the same reasons we dismiss paragraph V A.

Young & Rubicam's final objection is to order paragraphs V B and V C. (Young & Rubicam Appeal Brief pp. 10-12) These provisions would prohibit Young & Rubicam from referring to aspirin by any name other than aspirin and would require advertisements to disclose that Excedrin and Excedrin P.M. contain aspirin. Young & Rubicam argues that these provisions are not appropriate unless it can be shown that respondent knew or had reason to know that: (1) aspirin is a health hazard; (2) consumers are unaware that Excedrin and Excedrin P.M. contain aspirin; and (3) the presence of aspirin constitutes a material fact, the knowledge of which is likely to affect consumers' purchasing decisions. Further, Young & Rubicam argues that since it reasonably relied on substantiation provided by Bristol-Myers regarding Excedrin's safety, it cannot be shown that it knew or had reason to know that aspirin is a health hazard.

We are unable to agree with Young & Rubicam's formulation of the law. First, no ad for Excedrin discloses the presence of aspirin and several ads actually create the impression that Excedrin does not contain aspirin. (See *supra* pp. 51-52) Second, as we explained in our discussion of the liability of Ted Bates, Inc., it is only necessary for complaint counsel to show that respondent Young & Rubicam knew or had reason to know that the presence of aspirin in Excedrin constituted a material fact (*supra* p. 62). That respondent had or should have had such knowledge is demonstrated by the advertising campaign it created for Excedrin, a campaign based upon ads which create the impression that Excedrin does not contain aspirin. For this reason, we have entered order provisions similar to Paragraphs V B and C of the ALJ's order.

VIII RELIEF

The order which we enter in this case proscribes the violations committed by the three respondents and also encompasses related violations, the prohibition of which we believe is

necessary in order to prevent respondents from violating the law in the future. *FTC* v. *Ruberoid Co.*, 343 U.S. 470, 473 (1952); *American Home Products*, 98 F.T.C. at 398. This order diverges substantially from the order entered by the ALJ. First and foremost, the ALJ's order requires that any ad containing a comparative performance claim for an internal analgesic must either be substantiated by clinical tests or must contain a notice reflecting the lack of such substantiation. Our order imposes a clinical testing requirement only for those ads which claim that the analgesic's comparative superiority has been scientifically established. Second, the ALJ's order imposes a reasonable basis requirement on all efficacy or side effects claims respondent makes regarding *any* OTC drug. We have limited this provision so that it applies only to analgesics. Third, our order narrows the scope of the aspirin disclosure requirement imposed by the ALJ, limiting the disclosure of the presence of aspirin to those ads for analgesics which contrast the product with other aspirin-containing products. Also, our order does not cover labeling but is limited to advertising claims.

The order we have entered also requires Bristol-Myers to cease representing that common ingredients are unusual or special and to cease representing that any group recommends a product unless respondent possesses a reasonable basis for such claim.

With respect to the advertising agencies, the order will prohibit both Ted Bates & Company and Young & Rubicam, Inc. from representing that any nonprescription internal analgesic contains an unusual or special ingredient when such is not the case. This is an expansion of the ALJ's order, which only imposed the requirement on ads for Bufferin, Excedrin, and Excedrin P.M. In addition, both agencies are required to disclose in advertisements contrasting analgesics with aspirin that the product contains aspirin. Finally, Ted Bates will be prohibited from representing that any group endorses an analgesic unless it possesses a reasonable basis for making the claim.

A. Establishment Claims

Part I of the order sets forth the level of substantiation which Bristol-Myers must possess before it can advertise that the superior effectiveness or freedom from side effects of a nonprescription internal analgesic product has been established. Specifically, these ads must be substantiated by two adequate well-controlled clinical studies. The criteria for such studies are specified in Paragraphs A-C of Part I of the order; they represent the criteria which the record shows that the relevant expert community requires to establish a claim of superior performance or superior freedom from side effects (*supra* pp. 19-28).[93] Paragraph D of Part I provides that failure to comply with each and every specification of Part I will not result in a violation if Bristol-Myers can show that the substantiation it possesses would still be generally recognized by the scientific community as sufficient evidence to establish the truth of the claims. The purpose of this provision is to avoid penalizing Bristol-Myers for purely technical instances of noncompliance with the detailed provisions of Part I, if it can show that the scientific community would not regard the technical violations as affecting the measure of support for the claims provided by the tests.

Our decision in this case also explains in some detail which advertisements will trigger the clincial testing requirement. In brief, advertisements that claim the product's superiority has been proven or established or which create that impression through the use of visual aids and language must be substantiated by well-controlled clinical tests.[94]

This order applies the clinical testing requirement to establishment claims made by Bristol-Myers for any nonprescription internal analgesic product. Complaint counsel have argued that this requirement should apply not only to establishment claims promoting analgesics, but also to establishment claims made

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93 We applied the same testing requirement in the order which we entered against American Home Products Corp., 98 F.T.C. 136, 424-425.

94 See supra pp. 18-19.

by Bristol-Myers for any nonprescription drug. (CAB pp. 41-48) We reject complaint counsel's argument and we decline to extend the reach of this order provision beyond nonprescription internal analgesics. As we held in *American Home Products*, 98 F.T.C. at 402-403, it is possible that establishment claims for other drug products may be substantiated by other than two well-controlled clinical tests. On this point we find no reason to alter the decision we reached in *American Home Products*.

However, we do believe that this provision of the order should not be restricted merely to establishment claims for Bufferin and Excedrin. The appropriate breadth of this portion of the order is dependent upon a determination of the likelihood that the practices will be repeated. Factors that may be considered are the extent of the current violation, the transferability of the practice to other contexts, and whether the respondent has a past history of violations. *American Home Products*, 98 F.T.C. at 401; *see Sears, Roebuck and Co.* v. *F.T.C.*, 676 F.2d 385, 391-392 (9th Cir. 1982). But in the final analysis, we must look to the circumstances as a whole and not to the presence or absence of any single factor.

First, respondent's current violations were widely disseminated over several years on radio and television and in magazines at a cost of millions of dollars per year (F. 5).[95] Second, as we indicated in *American Home Products*, 98 F.T.C. at 401, it would be a simple matter for a manufacturer of analgesics to make inadequately substantiated establishment claims regarding other analgesics. Indeed, the prevention of this sort of transfer of an unfair trade practice is a proper goal of the Commission's remedial work. *Sears, Roebuck and Co.* v. *F.T.C.*, 676 F.2d at 394.

Respondent Bristol-Myers has an extensive history of dealings with the FTC which include the entry of three litigated

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95 In F.T.C. v. Colgate-Palmolive Co., 380 U.S. 374 (1965), an all products order was upheld based upon three different commercials produced by the respondent all of which employed the same deceptive practice.

orders[96] and the acceptance of seven stipulations[97] based upon false and deceptive advertisements. The first two litigated orders applied only to the specific product which had been falsely and deceptively advertised. However, in 1967 the Commission found that Bristol-Myers (through its Grove Laboratories Division) had disseminated false and deceptive advertisements regarding "Pazo Formula," a hemorrhoid preparation and we entered a two-part order, one part which applied to advertisements for any hemorrhoid preparation. We noted that:

> . . . we are convinced that we would be derelict in our responsibilities if we were to limit the prohibitions of the order against false representations solely to hemorrhoidal preparations having the same or similar ingredients. The ease with which such orders can be avoided has been amply demonstrated by the Commission's experience with this respondent alone. *Grove Laboratories, Inc.*, 71 F.T.C. 822, 847-848 (1967), *rev'd in part* 418 F.2d 489 (5th Cir. 1969).

Furthermore, in a 1968 proceeding we found that ads placed by Bristol-Myers misrepresented the freedom from side effects of Bufferin. *Bristol-Myers Co.*, 74 F.T.C. 780 (1968). We entered no order at that time but merely admonished Bristol-Myers to

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96 Bristol-Myers Co., 36 F.T.C. 707 (1943) (false and deceptive advertising claims regarding the laxative "Sal Hepatica"); Bristol-Myers Co., 46 F.T.C. 162 (1949), *aff'd* 185 F.2d 58 (4th Cir. 1950) (false therapeutic claim for "Ipana" toothpaste and false claim that dentists recommend it); Grove Laboratories, Inc., 71 F.T.C. 822 (1967), *rev'd in part*, 418 F.2d 489 (5th Cir. 1969) (false and deceptive advertisements regarding "Pazo Formula," a hemorrhoid preparation).

97 24 F.T.C. 1546 (1937) (health claims regarding "Vitalis" hair oil); 24 F.T.C. 1554 (1937) (health claims regarding "Ipana" toothpaste); 24 F.T.C. 1558 (1937) (health claims regarding the laxative "Sal Hepatica"); 25 F.T.C. 1626 (1937) (health claims for an alleged cold remedy, "Minit-Rub"); 27 F.T.C. 1602 (1938) (false claims for "Ingram's Milkweed Cream"); 27 F.T.C. 1609 (1938) (health claims for "Ingram's Shaving Cream"); Bristol-Myers Co., 47 F.T.C. 1441 (1950) (complaint dismissed and stipulation accepted regarding an alleged cold remedy, "Resistab").

heed the guidance of the opinion and to avoid disseminating misleading advertisements. Given this history and the facts of this case, we believe that the order provisions should fully address the kinds of claims and products at issue here. Although we are in no position to extend the requirement that establishment claims be substantiated by two well-controlled clinical studies to all drugs, it is entirely reasonable to extend the order to establishment claims made for all nonprescription internal analgesics.

Respondent Bristol-Myers argues that the requirements of Part I of the order would unconstitutionally abridge its First Amendment free speech rights. It contends that the substantiation requirement may "chill" protected truthful speech. (R.A.B. p. 12, 14, 69-74) However, the Supreme Court has made it clear that the First Amendment does not protect false advertising. *Va. State Board of Pharmacy* v. *Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 771 (1976). Since we have found that respondent falsely represented that the superiority of its products had been established, there is no constitutional impediment to an order provision prohibiting such false advertising in the future.

Respondent argues that *Friedman* v. *Rogers*, 440 U.S. 1 (1979), prevents imposition of a substantiation requirement. It argues that *Friedman* would protect from regulation truthful advertising. (R.A.B. pp. 66-70) We are unable to agree with Bristol-Myers' interpretation of that case. *Friedman* upheld against constitutional challenge a total ban on the use of trade names by optometrists. Although the Court pointed out that truthful commercial speech, such as price advertising by pharmacists, was entitled to constitutional protection, it stressed that "much commercial speech is not provably false, or even wholly false, but only deceptive or misleading. We foresee no obstacle to a State's dealing effectively with this problem." *Friedman*, at 9-10. The substantiation which we require in Parts I and II of this order is a constitutionally appropriate remedy designed to curtail Bristol-Myers' false and deceptive ads. Indeed, a reasonable substantiation requirement fosters rather than impairs First Amendment objectives because it

helps to insure that claims are reliable. *Jay Norris Corp.*, 91 F.T.C. 751, 851-855 (1978), *aff'd* 598 F.2d 1244 (2d Cir. 1979), *cert. denied* 444 U.S. 980 (1979). Thus, we see no constitutional bar to these parts or to any other part of the order we enter today.

B. Reasonable Basis Provision

Paragraph II of our order requires respondent to possess a reasonable basis for all therapeutic performance and freedom from side effects claims regarding OTC internal analgesics. In those instances in which Bristol-Myers represents that such claims have been established, paragraph I of this order applies. However, in those instances in which respondent makes a "non-establishment" performance or side effects claim, this provision of the order imposes on respondent the more general reasonable basis standard of substantiation.

The order entered by the ALJ would have imposed a similar requirement for claims regarding *any* OTC drug. While we are not willing to go this far, we believe that a reasonable basis requirement is appropriate for all future OTC analgesic claims. Most of the claims in this case were establishment claims and we found that Bristol-Myers did not possess adequate substantiation for any of these claims.[98] Our concern is that this violation, the making of inadequately substantiated claims, can easily be transferred to other sorts of claims, including non-establishment claims. In addition, the number and frequency of such violations, combined with the other factors (such as the history of past violations) discussed in the previous section, make it clear that order Paragraph II represents a fencing-in requirement that is reasonably related to the violations.

Moreover, some of the claims in this case were in fact judged under the "reasonable basis" standard (because they were not

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98 Even if respondent had not represented that its claims had been scientifically established, we might still have found that respondent lacked a reasonable basis for many of the claims. For example, respondent produced no evidence at all in support of its claim that Bufferin would not upset a user's stomach.

embellished with establishment representation), and respondent's evidence was again found wanting. At least 11 of respondent's ads represented that Bufferin relieves tension, and another ten ads made similar claims for Excedrin.[99] These violations alone could well justify a reasonable basis requirement extending to all products or all claims. *See, e.g., F.T.C.* v. *Colgate-Palmolive Co.,* 380 U.S. 374; *National Dynamics Corp.* v. *F.T.C.*, 492 F.2d 1333; *Sears, Roebuck & Co.* v. *F.T.C.,* 676 F.2d 385. Instead, we have limited the reasonable basis requirement here to therapeutic performance and freedom from side effects claims for OTC analgesics—*i.e.*, to the exact kinds of claims and products that were involved in this case.

Paragraph II thus has a much closer relation to the violations than did the reasonable basis provision that was deleted on appeal in *American Home Products* v. *F.T.C.,* 695 F.2d at 710-711. That provision was much broader in its product coverage, applying to all nonprescription drugs manufactured by American Home Products, including such products as topical anesthetics, antacid powders, hemorrhoid preparations, wart removers, denture cleansers, medicated shampoos, acne medications, corn removers, depilatories and breath fresheners. By contrast, Paragraph II of this order applies only to Bristol-Myers' OTC internal analgesics, the exact type of product involved in this case. According to information submitted by respondent to the 1982 edition of the *Physicians' Desk Reference,* respondent makes only 10 different OTC internal analgesics.

In general, the amount of substantiation necessary to constitute a reasonable basis must be determined case-by-case. In part for that reason, and in part because we did not evaluate all of the claims in this case under a reasonable basis standard, the order does not describe in detail the amount and kinds of evidence necessary to constitute a reasonable basis for Bristol-Myers' future claims. It is clear, however, that two well-controlled clinical tests, the amount of evidence necessary to

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99 See supra pp. 44-46.

establish a claim, would constitute a reasonable basis for any therapeutic performance or side effects claim. Thus, Paragraph II states that that amount of evidence will be deemed to provide a reasonable basis for such claims.

Whether any lesser amount of evidence could also constitute a reasonable basis is more difficult to determine. The experts who testified in this case indicated that the scientific community requires two well-controlled clinical tests to evaluate therapeutic claims. Thus, even if some lesser amount of evidence were appropriate for non-establishment claims, it is difficult to see where that level could possibly be set. Nonetheless, we cannot rule out the possibility that other types of evidence might be adequate on the record before us in this case.[100] Accordingly, order Paragraph II does permit respondent to substantiate its claims with evidence other than two clinical tests if it can show that such evidence is sufficiently reliable to support a good faith belief in the truth of the claim. Such a showing must be based on the factors set forth in the *Pfizer* line of cases—the nature of the claim, the degree of consumer reliance on the claim, the consequence to consumers if the claim is, in fact, false, and the accessibility of various types of evidence.

Concededly, permitting such a showing creates some ambiguity regarding the absolute minimum amount of evidence necessary to provide a reasonable basis for respondent's future claims. But this is inherent in any reasonable basis order by virtue of the factors set forth in *Pfizer.* As we noted in that case, the reasonable basis standard can only be determined on a case-by-case basis. 81 F.T.C. at 64. Indeed, it is settled that Commission orders are required only to be "as specific as the circumstances permit," *F.T.C.* v. *Colgate-Palmolive Co.*, and

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100 A different standard of evidence might be appropriate for different types of claims. For example, in some situations the FDA will permit a drug to be marketed without clinical testing if non-clinical tests show the drug to be as effective as another drug whose effectiveness has already been established by clinical tests. See 45 Fed. Reg. 77807-08 (1980). However, this non-clinical evidence is used to show that the drugs are equivalent, not that one is superior to another.

courts have upheld reasonable basis requirements, including those in orders having broader coverage than this one. *E.g., Sears, Roebuck and Co.*

In fact, in this case there are several methods whereby Bristol-Myers can resolve uncertainty regarding the level of substantiation required by the order. First, it can be assured of compliance with the order by conducting two well-controlled clinical tests as described in Paragraph I. Second, pursuant to Rule 2.41(d) of the Commission's Rules of Practice, Bristol-Myers may seek an advisory opinion from the Commission. Third, even if Bristol-Myers does not possess adequate support to constitute a reasonable basis for a broad, unqualified claim, it may still make the claim by carefully qualifying it so that it discloses the level of support actually possessed. As we have indicated in numerous cases, we require advertisers to possess a reasonable basis for their claims because that is what consumers expect and they will be deceived if that level of support does not exist. *See, e.g., Porter & Dietsch, Inc.*, 90 F.T.C. 770; *National Dynamics Corp.*, 82 F.T.C. 488. This deception can be avoided if the ad is properly qualified so that consumers know the nature and limitations of the support the advertiser actually possesses for the claim.

For the above reasons, we believe that the relief provided by Paragraph II is directly related to Bristol-Myers' violations and that it adequately balances the goals of preventing future violations and providing Bristol-Myers with notice as to what conduct is prohibited.

C. Ingredient Claims and Omissions

As we explained above, Bristol-Myers' advertisements falsely represent that "Bufferin" and "Excedrin" contain special or unusual ingredients. (*Supra* pp. 49-52) Under Part III A of the order, Bristol-Myers may not represent that a product contains any special or unusual ingredient when that ingredient is commonly used in other nonprescription drug products for the same purpose. To determine the scope of this section of the order, we have applied the same considerations discussed in connection with Part I and Part II. The violations in this case

are extensive and respondent Bristol-Myers has a history of past dealings with the Commission. These facts justify broad coverage. Furthermore, the practice of falsely representing that ingredients are unusual could easily be applied to other drug products. Indeed, two of the stipulations entered in the past by Bristol-Myers required it to cease and desist from representing that its drugs contained unusual ingredients. In the first of these stipulations, Bristol-Myers agreed to cease and desist representing that the cold remedy "Minit-Rub" was a special analgesic or contained drugs other than those commonly used in analgesics. 25 F.T.C. 1626 (1937). The second stipulation required Bristol-Myers to cease representing that a facial cream, "Ingram's Milkweed Cream," contained special ingredients not found in other creams. 27 F.T.C. 1602 (1938). For these reasons, Part III A of the order applies to advertising for any nonprescription drug product.

Part IV of the order differs substantially from Part III A. The latter provision prohibits respondent from falsely representing that its analgesics contain special or unusual ingredients. The purpose of the paragraph IV is to prevent respondent from passing off its aspirin-based analgesic products as being different from aspirin or from otherwise misrepresenting the identity of any analgesic ingredient. The principal means by which this deception has been accomplished in the past has been to contrast some unspecified analgesic ingredient in respondent's product with aspirin, or with the ingredient in a competing aspirin-based analgesic. Such a contrast inevitably implies that the unidentified analgesic ingredient in the first product is different from aspirin. To prevent this practice, paragraph IV prohibits any misrepresentation that the analgesic ingredient in an aspirin-containing product is different from aspirin. To prevent closely related violations, the order prohibits misrepresentations regarding the identity of any analgesic ingredient in respondent's products. The order also makes clear that any attempt to contrast the ingredient in an aspirin-based analgesic without disclosing that the ingredient in respondent's product is aspirin will violate the order.

This aspirin disclosure requirement differs from the comparable provision in the order entered by the ALJ which would have required this disclosure in any ad for an aspirin-based analgesic. We are unprepared to state on the basis of the record in this case that the mere failure to disclose the presence of aspirin in an advertisement for an analgesic is an unfair or deceptive practice. However, respondent Bristol-Myers' advertising was deceptive because it contrasted its own aspirin-based analgesics with other aspirin-based products without disclosing the presence of aspirin in its products. This created the false impression that the analgesics advertised did not contain aspirin. The disclosure required by this part of the order will prevent this deceptive sort of comparison. Indeed, it is possible that without a provision such as this one, respondent would devise new ways to capitalize on the public's ignorance of the ingredients in Bufferin and Excedrin. *See American Home Products* v. *F.T.C.*, 695 F.2d at 712.

D. "Doctors Recommend" and Tension Relief Claims

Part III B of the order is necessary in light of our finding that Bristol-Myers falsely represented that doctors recommend Bufferin more than any other nonprescription internal analgesic. It will prohibit Bristol-Myers from representing that any group recommends any nonprescription drug product unless Bristol-Myers possesses a reasonable basis for making such a claim. This order provision applies to any nonprescription drug product because this sort of representation easily could be made about any product and respondent has made similar representations in the past regarding toothpaste.[101]

E. Corrective Advertising

Corrective advertising is a remedy available to the Commission to correct misleading impressions created by previous

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101 Bristol-Myers agreed in a stipulation to cease representing that dentists usually prescribe "Ipana" toothpaste to patients with gum disorders. 24 F.T.C. 1554 (1937). In a subsequent litigated order, Bristol-Myers was required to cease representing that more dentists recommend "Ipana" than any other two toothpastes combined. Bristol-Myers Co., 46 F.T.C. 162 (1949).

advertising. *Warner-Lambert Co.* v. *F.T.C.*, 562 F.2d 749, 756-759 (D.C. Cir. 1977), *cert. denied,* 435 U.S. 950 (1978). Two inquiries must be made in order to determine if the remedy is appropriate: (1) did the advertisements in question play a substantial role in creating or reinforcing a false belief in the public's mind regarding the product; and (2) will the belief remain after the advertising ceases? *Warner-Lambert Co.* v. *F.T.C.*, Id. at 762. Complaint counsel devote a substantial portion of their appeal brief to a request that we include a corrective advertising requirement in the order which we enter against Bristol-Myers. (CAB pp. 12-39) They argue that absent such relief, consumers will continue to believe that Bufferin's and Excedrin's comparative superiority have been established. The ALJ was unwilling to conclude that consumers have an image of *established* superiority for Bufferin and Excedrin. I.D. p. 251) However, complaint counsel contend that this image may be inferred from the challenged advertisements or from consumers' expectations regarding the substantiation which an advertiser should possess prior to comparing one analgesic to another. They also contend that the presence of the image is demonstrated by consumer research in the record.

It is our conclusion that corrective advertising is not a proper remedy in this case. Although we have found that numerous ads do represent that Excedrin's and Bufferin's superiority have been established, we decline to infer that that image will persist. While the record does demonstrate that the public has held the belief that Bufferin and Excedrin are superior to aspirin (F. 757), there is no evidence that consumers will retain an image that this superiority has been established. Finally, we will not infer that the public will retain an image of *established* superiority from the fact that it currently has an image of Bufferin's and Excedrin's superiority. As we explained above (*supra* pp. 40-41), we are unwilling to conclude that consumers believe that advertisers possess the degree of substantiation for every comparative performance claim which would satisfy relevant experts.[102] Indeed, we have reached no conclusion as

102 Compare Warner-Lambert Co. v. F.T.C. in which survey evidence showed that consumers would retain a false image regarding Listerine. 562

to whether Bristol-Myers did or did not possess a reasonable basis for its comparative performance claims. Thus, we cannot infer from the record that an establishment image will persist and, therefore, corrective advertising is an inappropriate remedy.

F. Labeling

The order entered by the ALJ would apply not only to respondents' advertising, but also to the labeling for its products. As we stated in *American Home Products,* 98 F.T.C. at 411, our liaison agreement with the FDA recognizes that primary responsibility for the labeling of nonprescription drugs rests with it. For the reasons set forth in that opinion, the order which we enter does not apply to labeling.

G. Advertising Agencies

The extent of the liability of Ted Bates & Company, Inc., and Young & Rubicam, Inc., has been discussed above (*supra* pp. 58-65), and we have entered appropriate order provisions regarding the two advertising agencies. The order prohibits both agencies from falsely representing that an advertised analgesic contains an unusual or special ingredient and requires both agencies to disclose presence of aspirin in an analgesic when an ad contrasts the product's analgesic ingredients with aspirin. In addition, Ted Bates may not represent that any group endorses a product unless it has a reasonable basis for the representation.

The order provisions regarding the advertising agencies apply to ads for any nonprescription internal analgesic. The deceptive practices employed by the respondents could easily be used in advertisements for other analgesics. It is, therefore,

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F.2d at 762. We note that survey evidence is only one factor to be considered in determining whether corrective advertising is appropriate in a particular case. Other factors to be considered are the amount of exposure consumers have had to the false claim, the persuasive characteristics of the claim, the manner in which the claim is presented, and the nature of the audience. Even considering all of these factors, we do not think corrective advertising is appropriate in this case.

essential that we enter an order which will prevent this. *ITT Continental Baking Co., Inc.* v. *F.T.C.*, 532 F.2d at 222. In addition, respondent's violations were not isolated instances but were the basis of extensive advertising campaigns. For these reasons, our order applies to ads for all analgesics.[103]

IX CONCLUSION

For the reasons set forth above, the initial decision of the administrative law judge is modified as described. An appropriate order is appended.

ISSUED: July 5, 1983

CONCURRING STATEMENT OF CHAIRMAN MILLER

I concur with the decisions reached by the majority in these two cases and wish to compliment Commissioner Clanton for his thorough review of the records and for his insightful commentary. But while joining in the majority decisions, I wish to note three caveats.

First, although I agree with the outcomes of these cases, including the individual charges of liability, I do not necessarily agree with each and every argument that is advanced. This is, of course, an occupational hazard. Majority decisions are inherently "consensus documents" and should be read with that in mind.

Second, in a particular application of the point just made, I take issue with the majority's differentiating between an "establishment claim theory" and a "reasonable basis theory." To

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103 In addition, twice in the past Ted Bates has had litigated cease and desist orders entered against it. ITT Continental Baking Co., Inc., 83 F.T.C. 865, (misrepresentations regarding the extent to which Wonder Bread contributes to growth); Colgate-Palmolive Co., 59 F.T.C. 1452 (1961), *remanded* 310 F.2d 89 (1st Cir. 1962), *remanded* 326 F.2d 517 (1st Cir. 1963), *rev'd reinstating Commission's order,* 380 U.S. 374 (1965) (use of mock-ups to falsely prove the quality of shaving cream).

me, the overarching goal of our law enforcement efforts in this area is to encourage truthful advertising; specifically, to eliminate unfairness and deception. The Commission's celebrated, and controversial, reasonable basis standard, first enunciated in *Pfizer* over a decade ago, is a useful tool for the Commission in achieving that end. I am troubled by any communication, such as that implicit in these opinions, that the Commission will apply one standard (i.e., reasonable basis) in cases generally, and another standard (e.g., establishment claim) in specific situations. Rather, I would encourage the Commission to consider whether the reasonable basis test, or some variant of it, were not the appropriate standard for universal application, thus reducing uncertainty in the private sector and, possibly, avoiding double jeopardy.

Third, because of the importance of these cases it would have been desirable to have the benefits of the Commission's review of its ad substantiation program, as well as the staff's efforts to develop a protocol defining deception, before these cases were made final. However, I am well aware that both cases are over a decade old and agree with the adage, "Justice delayed is justice denied." Thus, I believe that expeditious treatment of these opinions wins out in any weighing of the equities. This is not to say, of course, that in the future the Commission should not articulate a somewhat different, more comprehensive, standard for claims of these types.

ISSUED: July 5, 1983

SEPARATE STATEMENT OF COMMISSIONER PERTSCHUK CONCURRING IN PART AND DISSENTING IN PART

I concur with most of the Commission's Opinion and Order. For the reasons discussed below, however, I cannot join with the majority's decision to reverse the "substantial question" doctrine announced so recently in *American Home Products Corporation*, 98 F.T.C. 136 (1981), *aff'd*, 695 F.2d 681 (3d Cir.

1982). Accordingly, I dissent from the Commission's decision to dismiss paragraphs 9 through 11 and 14 through 16 of the complaint.

Together with our opinion in *Sterling Drug, Inc.* (D. 8919), also announced today, these three cases represent the culmination of a decade-long attempt to curb allegedly deceptive advertising in the multi-million dollar over-the-counter ("OTC") aspirin-based pain reliever market. That deception, now documented by three lengthy adjudicative records, has stemmed from a marketing strategy, adopted by each of the major makers of pain relievers named in these cases, to portray *their* particular pain reliever as being different and more effective than any other, including plain aspirin. Unfortunately, such a strategy is at its heart deceptive, since the most assiduous efforts of company counsel in each of these three cases have failed to unearth conclusive evidence that any one aspirin-based product is in fact any better than any other in doing what people buy analgesics for—relieving pain. As a result, the claims made by these leading makers that there are differences in effectiveness among aspirin-based pain relievers have largely been a fraud on the American public.

In *American Home Products*, the Commission found unequivocal claims of analgesic superiority made by American Home Products ("AHP") for Anacin to be deceptive. There, we required AHP to refrain from such claims unless it either proved through two well-controlled clinical tests that in fact Anacin was more effective in relieving pain, or else disclosed that there was a "substantial question" about the claim.

The analysis used to reach that decision was straightforward. First, the Commission considered the context in which consumers are exposed to claims for OTC pain relievers. Taking notice of the public's concern with the special health risks associated with therapeutic drug products, the inability of the public to verify objectively the consequences of therapeutic drug use, and the reasonable consumer expectation that the marketing of drug products claims is carefully regulated by the government, the Commission held that:

> when an advertiser has made unequivocal, unqualified claims about a drug product's effects . . . consumers may be led to expect, quite reasonably, that the claims are supported by meaningful evidence, of the sort that would be likely to satisfy the relevant scientific community. *American Home Products, supra*, at 386.

The Commission then determined that the scientific community considers one analgesic drug to be more effective than another only when its superiority is demonstrated by two well-controlled clinical tests. *Id.* at 373-381. In the absence of such supporting evidence, the scientific community would view any such claim as being open to doubt. Since AHP had no such tests to support its claims, and therefore did not possess the level of proof consumers reasonably would expect, the Commission held that it was deceptive for AHP to claim that Anacin was more effective than other OTC internal analgesic drug products, without qualifying the claim by disclosing that there was a substantial question about its validity. The Commission's findings, analysis, and order addressing this problem were affirmed by the Third Circuit in a well-reasoned and scholarly opinion. *American Home Products* v. *FTC*, 695 F.2d 681 (3d Cir. 1982)[1]

The majority in today's opinion retreats from the "substantial question" principle established in *American Home Products*. In doing so, the majority argues that the substantial question analysis eliminates any difference between "establishment claims" (claims which refer to scientific proof), and "superior efficacy claims" (claims which do not refer to any type or quality of proof). The majority rejects the assumption made by the Commission in *American Home Products* that an unequivocal superior efficacy claim could reasonably lead consumers to believe that it was supported by scientific proof. In the majority's view, the difficulty with that assumption is that "there has never been any evidence to confirm this somewhat counterintuitive reading of consumer expectations." Slip op. at 40.

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1 The Third Circuit reversed one subparagraph portion of the Commission's Order which is not relevant here.

The absence of extrinsic evidence about consumer expectations has never barred the Commission from making informed, considered judgments about what consumers could reasonably be expected to believe about a given claim. As the courts have recognized, "[d]etermining whether an advertisement is deceptive draws upon the FTC's familiarity with the public's expectations." *Litton Indus., Inc.* v. *FTC*, 676 F.2d 364, 369 (9th Cir. 1982). Indeed, underlying the "reasonable basis" doctrine itself is the fundamental proposition that "consumers are likely to assume that when a product claim is advanced which is in theory subject to objective verification, the party making it possesses a reasonable basis for so doing, and that the assertion does not constitute mere surmise or wishful thinking on the advertiser's part." *Nat'l Commission on Egg Nutrition*, 88 F.T.C. 89, 193 (1976), *modified*, 570 F.2d 157 (7th Cir. 1977), *cert. denied*, 439 U.S. 821 (1978). Absent any reference in a claim to the evidence on which the claim is based, the Commission routinely assumes that consumers expect advertisers to possess and rely upon whatever type of evidence is appropriate to substantiate the claim. It does not require extrinsic evidence of those expectations, although such evidence, if produced, will be considered. *See, e.g.*, *Fedders Corp.*, 85 F.T.C. 38 (1975), *aff'd*, 529 F.2d 1398 (2d Cir.), *cert. denied*, 429 U.S. 818 (1976); *Sears, Roebuck & Co.*, 95 F.T.C. 406 (1980), *aff'd*, 676 F.2d 385 (9th Cir. 1982); *Jay Norris*, 91 F.T.C. 751 (1978), *modified*, 598 F.2d 1244 (2d Cir.), *cert. denied*, 444 U.S. 980 (1979).

If it is reasonable to find without extrinsic evidence proof that consumers expect claims to be supported by evidence sufficient to substantiate the claim, it seems hardly "counterintuitive" to find similarly that consumers expect claims comparing the medical benefits of various drugs to be supported by appropriate scientific evidence. In affirming the Commission's decision in *American Home Products*, the Third Circuit upheld that assumption, noting:

> Of course the Commission is not committed to the unrealistic notion that consumers understand the clinical

> details of comparative drug testing or the exact mechanisms of government regulation. It merely asserts that consumers reasonably assume that the proper governmental authorities will take steps to ensure that unqualified claims of a drug's superiority are supported by whatever proof the appropriate medical or scientific experts consider sufficient. *American Home Products* v. *FTC*, 695 F.2d 681, 698 (footnotes omitted).

Indeed, the Commission's analysis of the "establishment" claims in the instant case rests on an assumption about consumer expectations scarcely distinguishable from that made by the Commission in *American Home Products*. No proof was offered in these cases that consumers understand a mere reference to a scientific test or a computer print-out to mean the claim has been established as scientific fact to the satisfaction of the relevant scientific community. Nevertheless, the Commission today assumes that consumers could reasonably be led to believe from direct and indirect references to a scientific study in ads for Bufferin and Excedrin that "the scientific community regards Bufferin and Excedrin to be superior." Slip op. at 19. The only justification for this assumption is the observation that "[w]here scientific evidence is cited in support of a claim, absent some explicit qualification it is unlikely that consumers would interpret such evidence narrowly to provide proof for only a limited portion of the claim." *Sterling Drug*, *supra*, slip op. at 13, note.

It appears, then, that the Commission is willing to make assumptions about consumer expectations which are certainly as reasonable as the assumption that consumers expect therapeutic efficacy claims for drugs to be scientifically supported. The majority's concern about *American Home Products* therefore seems to stem not so much from the "unreasonableness" of the assumption made there as from a concern about the scope of that theory. In the majority's view, the same factors cited by the Commission in *American Home Products* in support of the assumption that consumers reasonably expect superior therapeutic efficacy claims to be backed by scientific

proof would exist with respect to *any* drug performance claim. As a result, application of that assumption, according to the majority, would necessarily lead the Commission to require all drug performance claims to be backed by two well-controlled clinical tests.

While the Commission's opinion in *American Home Products* was carefully limited to the facts in that case,[2] I believe it is entirely appropriate for the Commission to assume consumers generally expect therapeutic efficacy claims for drugs to be supported by scientific fact. In an age when consumers are told that drugs are constantly monitored by the government and industry through careful scientific tests for safety and efficacy, consumers quite reasonably expect drug products to provide the therapeutic benefits claimed for them. This belief is particularly justified because consumers are frequently unable to determine the therapeutic value of a drug for themselves by simply using it. They do not expect such claims to be based on hunches, or on informed guesses, or on untested scientific theories, but on accepted scientific fact.

While the Commission's rationale for adopting the substantial question doctrine in *American Home Products* is, at least in my view, applicable generally to any therapeutic efficacy claim for an OTC drug, it does *not* follow—as the majority implies—that all such claims must be supported by the strict two well-controlled clinical test standard which the Commission adopted in *American Home Products*. As the majority recognizes, the Commission does not depend on consumer expectations to determine precisely what type of evidence is necessary to substantiate a given claim. Slip op. at 41. Determining the appropriate level of evidence is essentially a factual inquiry, one which must weigh a number of considerations and which can only be determined on a case-by-case basis. *Pfizer, Inc.*, 81 F.T.C. 23, 64 (1972). Consequently, we might find from the facts in a different case that a level of proof less than the two well-controlled clinical test standard would be appropriate for other types of drug product therapeutic efficacy claims.

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2 *See, American Home Products* v. *FTC, supra*, 695 F.2d at 701.

The majority's decision, unfortunately, may leave unsolved the central problem that our trilogy of analgesics cases was designed to address—the profusion of mutually inconsistent claims by analgesic makers that each produces the most effective pain reliever. By refusing to extend the "substantial question" doctrine to these cases, the Commission creates unnecessary uncertainty about what evidence each maker has to possess to claim that its product is the best pain reliever. Under today's order, the makers must substantiate such claims with "competent and reliable scientific evidence." While the opinion makes clear that two well-controlled clinical tests suffice to meet that standard, and suggests further that such tests may well be the *only* data which could meet such a standard, the opinion expressly leaves open the question whether evidence short of such tests would be sufficient. (Slip op. at 71-72) That uncertainty creates a potential for Bristol-Myers to claim that Excedrin is more effective than Anacin or Bayer aspirin, and for Sterling Drug to claim that Bayer aspirin is more effective than Excedrin or Anacin. And American Home Products, should the substantial question provisions of the order against it be modified, in fairness, to conform to the Commission's order here, may be able to claim that Anacin is more effective than Bayer aspirin or Excedrin. Purely as a matter of logic, only one of these advertisers can possibly be telling the truth. And the chances are that *none* is—because the evidence in these three cases suggests that there is probably no clinically significant difference among any of these products.

ISSUED: July 5, 1983

SEPARATE STATEMENT OF COMMISSIONER PATRICIA P. BAILEY CONCURRING IN PART AND DISSENTING IN PART

BRISTOL MYERS, Docket No. 8917
&
STERLING DRUG, Docket No. 8919

The Commission today has issued the last two opinions in a three-part series of cases challenging the national advertising of several major over-the-counter (OTC) analgesics products. In both cases, I concur in the majority's findings of liability, as far as they go. However, because portions of the Commission's *American Home Products** decision are overturned by the decisions issued today, I must register my dissent from those aspects of *Bristol Myers* and *Sterling* which are inconsistent with the holdings in *American Home Products*.

In that earlier opinion, the Commission concluded that any claim that Anacin was more effective than any other OTC analgesic implied that such a claim was "established" by evidence generally acceptable to the scientific community. Therefore, we decided, it was deceptive to make such a claim unless the advertiser possessed adequate substantiation for it. Having ruled in that opinion (and in these) that an "establishment" claim requires substantiation by two competent and reliable clinical tests, the same substantiation level was required in *American Home Products* when comparative performance claims were made. Absent possessing such substantiation, the advertiser would have to disclose the existence of a "substantial question" as to the comparative effectiveness claim.

In these two opinions today, the Commission reaffirms its decision in *American Home Products* that an "establishment" claim requires substantiation by two competent and reliable clinical tests. But the majority here decides that this two-test substantiation requirement will not be triggered by "establish-

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* American Home Products Corporation, 98 F.T.C. 136 (1981), *aff'd* 695 F.2d 681 (3rd Cir. 1982).

ment" implications inherent in a comparative performance claim. Instead, these opinions hold that the two-test requirement will only be triggered when the advertiser makes affirmative express or implied claims that its product's effectiveness has been "established".

I disagree with the majority's limitation of the estalishment theory in this way and dissent from its decision to dismiss those portions of the complaint in these two cases which depend on the original theory articulated in *American Home Products.* As the Third Circuit stated in upholding the Commission's decision in *American Home Products:*

> Pervasive government regulation of drugs, and consumer expectations about such regulation, lend drug claims all the more power to mislead. The Commission's reasoning on this point . . . . is similar to that approved in *Simeon Management Corp.* v. *FTC.* . . . The Commission in these proceedings reasonably extended the ideas approved in *Simeon* from prescription to non-prescription drugs, and from absolute representations about safety and effectiveness to comparative representations. Non-prescription as well as prescription drugs are subject to the FDA's requirements that absolute safety and efficacy be demonstrated by well-controlled clinical tests. And the Commission concluded that many consumers could reasonably believe that the federal government demanded similarly high standards for claims of comparative effectiveness and safety as are imposed on absolute claims.
>
> Of course the Commission is not committed to the unrealistic notion that consumers understand the clinical details of comparative drug testing or the exact mechanisms of government regulation. It merely asserts that consumers reasonably assume that the proper governmental authorities will take steps to ensure that unqualified claims of a drug's superiority are supported by whatever proof the appropriate medical or scientific experts consider sufficient.

> Another consideration in favor of holding comparative effectiveness and safety claims for analgesics to high standards of substantiation is the difficulty for the average consumer to evaluate such claims through personal experience, and the consequent tenacity of advertising-induced beliefs about superiority. (emphasis in original) 695 F.2d at 697-698.

I would also note that the revised theory of liability adopted by the majority depends on the identification of express or implied establishment claims in an advertisment. The lines drawn by the majority providing guidance as to when such claims are present are exceedingly fine. Thus, the advertising industry is told that the depiction of a computer typewriter, by itself, does not constitute an establishment claim, but that the same visual, coupled with a certain kind of text, does (*Bristol Myers* Slip Op. at pgs. 10-11); that a mortar and pestle or glass figures of people with tablets crumbling in their stomachs do not communicate an establishment claim (*Sterling* Slip Op. at pg. 20, *Bristol Myers* Slip Op. at pg. 11), and that a pause between sentences of an otherwise questionable establishment claim may be enough to cure it of its establishment implication (*Bristol Myers* Slip Op. at pg. 12). At the same time, use of a visual depicting the product's chemical formula can convert the claim into an establishment claim. (*Bristol Myers* Slip Op. at pg. 18) All of this delicate line-drawing may well pose confusing problems of interpretation for those who must comply with the standards enunciated in these opinions and I hope the Commission will be able to provide necessary guidance to those who are perplexed.

Finally, I would hope some of the Commission's interpretations of particular advertisements are not carried too far and misinterpreted. In particular, while I do not disagree with Commissioner Clanton's analysis of the specific advertisements touting the superiority of the process used by Sterling in the manufacturer of various Bayer aspirin products, I believe these interpretations must be carefully confined to the entire context of the advertisements in question. (See *Sterling* Slip

Op. at pgs. 15 and 16.) Certainly, claims that an advertiser utilizes a special manufacturing process can often amount to a claim of superior efficacy and it would be most unfortunate if advertisers misinterpreted the opinion to permit such deceptive representations.

ISSUED: July 5, 1983

CONCURRING STATEMENT OF COMMISSIONER DOUGLAS

I concur in the Commission's finding of liability and its choice of remedies in these two matters. Commissioner Clanton's majority opinions have carefully analyzed the numerous specific claims addressed at trial. In my view, the majority opinions make a commendable effort to draw upon available evidence of consumer views in interpreting specific advertising claims. For the future, I hope the Commission will rely increasingly upon such extrinsic evidence in determining the meaning of advertisements when implied claims are at issue. The soundness of the interpretations the Commission ultimately adopts can be enhanced substantially by resort to evidence, beyond our individual and collective judgments, which suggests how consumers themselves interpret the advertisements in question.

Our experience with these cases also underscores the desirability of pleading future advertising cases more narrowly. The abundance and variety of claims raised by the complaints here appear to have hindered the expeditious adjudication of the relevant issues and encumbered the Commission's efforts to analyze the disputed claims. I expect that the Commission's ongoing examination of both its advertising substantiation program and the standards by which it identifies deception will produce important refinements in the way in which the agency pleads and decides advertising cases. This process of review and analysis may yield useful adjustments in the standards the Commission employs to evaluate advertising claims. While I

support the result achieved in these decisions, I do not endorse all elements of the reasoning in the majority opinions, nor do I foreclose the possibility of doctrinal changes as the Commission completes its review of its advertising enforcement program.

ISSUED: July 5, 1983

Order Denying Respondent Bristol-Myers' Petition For Reconsideration

UNITED STATES OF AMERICA
BEFORE FEDERAL TRADE COMMISSION

Docket No. 8917

COMMISSIONERS: James C. Miller III, Chairman
David A. Clanton
Michael Pertschuk
Patricia P. Bailey
George W. Douglas

In the Matter of

BRISTOL-MYERS COMPANY,
a corporation,

TED BATES & COMPANY, INC.,
a corporation, and

YOUNG & RUBICAM, INC.,
a corporation.

ORDER DENYING RESPONDENT BRISTOL-MYERS' PETITION FOR RECONSIDERATION

An opinion and final order in this matter were issued on July 5, 1983. Respondent Bristol-Myers was served with the opinion and order and petitioned for reconsideration thereof on August 8, 1983. The Commission, for reasons stated in the accompanying opinion, has determined to deny Bristol-Myers' Petition for Reconsideration. Therefore,

IT IS ORDERED, that Respondent Bristol-Myers' Petition for Reconsideration be, and hereby is, dismissed.

By the Commission.

/s/ EMILY H. ROCK

Emily H. Rock
Secretary

SEAL

ISSUED: October 14, 1983

Opinion of the Commission

UNITED STATES OF AMERICA
BEFORE FEDERAL TRADE COMMISSION

Docket No. 8917

COMMISSIONERS: James C. Miller III, Chairman
David A. Clanton
Michael Pertschuk
Patricia P. Bailey
George W. Douglas

In the Matter of

BRISTOL-MYERS COMPANY,
a corporation,

TED BATES & COMPANY, INC.,
a corporation, and

YOUNG & RUBICAM, INC.,
a corporation.

OPINION OF THE COMMISSION

By Clanton, Commissioner:

Respondent, Bristol-Myers Company ("Bristol") has filed a petition for reconsideration asking that the Commission delete two paragraphs of the order entered against it on July 5, 1983. Bristol asserts that Paragraph II of the order places the company at a competitive disadvantage and is excessively vague and not reasonably related to the violations giving rise to it. Bristol contends Paragraph III-A should be deleted because our order dismissed all the claims on which it was premised. In

addition, Bristol asserts that marketplace changes have eliminated entirely the need for the kind of relief ordered in the two provisions. For the reasons stated below, the petition is denied in its entirety.

Paragraph II

Paragraph II of our order reads in pertinent part:

> IT IS * * * ORDERED that respondent Bristol-Myers * * * do forthwith cease and desist from making any therapeutic performance or freedom from side effects claim for ["Bufferin", "Excedrin", or any other nonprescription internal analgesic] unless respondent possesses a reasonable basis for making that claim. A reasonable basis for such a claim shall consist of competent and reliable scientific evidence supporting that claim. Well-controlled clinical tests conducted in accordance with the criteria set forth in Order Paragraph I shall be deemed to constitute a reasonable basis for a claim.

Bristol contends that Paragraph II places it at an unwarranted competitive disadvantage vis-a-vis its competitor, American Home Products Corporation ("AHP"), because a "virtually identical" provision in the order we entered against AHP (Paragraph II(D)) was deleted by the Third Circuit on AHP's petition for review. See *American Home Products Corp.* v. *FTC* (*AHP*), 695 F.2d 681, 710-11 (3d Cir. 1982).

Preliminarily, we disagree that the two provisions are "virtually identical". The provision deleted on AHP's petition for review was directed to noncomparative representations of effectiveness or freedom from side effects of all over-the-counter drugs. By contrast, Paragraph II of the order in this case applies only to claims concerning the company's internal analgesics. It was this greater breadth of the AHP order that constituted one of the Third Circuit's objections to it.

Even more important is the fact that the only violation of the sort prohibited by Paragraph II(D) that AHP actually committed was covered by another provision in its order.

Moreover, the AHP order contains provisions not found in the Bristol order, and taken as a whole, provides protection against deceptive advertising at least as great. To delete the corresponding provision in this case would mean that the numerous nonestablishment performance and freedom from side effects claims made by Bristol (see slip op. at 7-17) would not be covered by any other provision in our order, and Bristol would be free to engage in deceptive advertising now foreclosed by order to its competitors.

Bristol next argues that Paragraph II is impermissibly vague because it does not specify the amount and kinds of evidence that are necessary to constitute a reasonable basis for future claims.

We believe that Bristol will have no difficulty in applying the requirements of Paragraph II to its contemplated future advertising. In its opinion the Commission construed the "reasonable basis" requirement of Paragraph II to mean "competent and reliable scientific evidence." We also specified a type of scientific evidence that will always satisfy that standard—*i.e.*, two well-controlled clinical trials* (Slip op. at 71). However, because we were unable to determine on the basis of the record whether some lesser standard might ever constitute a reasonable basis, we fashioned an order that allows Bristol to show in a given case that a lesser amount of support is adequate. Indeed, it is the advertiser who best knows the product and is best situated to verify the accuracy of claims made for it, *Sears Roebuck & Co.* v. *FTC*, 676 F.2d 385, 400 (1982). Should a situation arise in which Bristol is genuinely unable to determine whether two well-controlled clinical trials are required, it can, by complying with Rule 2.41(d) of the Commission's Rules of Practice and Procedure, obtain definitive advice as to whether its proffered substantiation would satisfy the order. See, *e.g.*,

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* Thus this case differs from *Standard Oil Co.* v. *FTC*, 577 F.2d 653 (9th Cir. 1978). There, the court of appeals rejected the Commission's suggestion that any vagueness could be cured by an advisory opinion because various paragraphs of the Commission's order simply restated general principles of fair advertising. 577 F.2d at 661.

FTC v. *Colgate-Palmolive Co.*, 380 U.S. 374, 392 (1965); *Jay Norris, Inc.* v. *FTC*, 598 F.2d 1244, 1251 (2d Cir. 1979).

Bristol's final objection to Paragraph II is that it is premised on too slender a basis—*i.e.*, the tension relief claims for Bufferin and Excedrin. In support of this argument it relies on the portions of the Third Circuit's opinion in *AHP* that explain why the one noncomparative tension-relief claim for Anacin did not justify imposing a reasonable basis requirement on all efficacy and freedom-from-side effects claims for all over-the-counter drugs.

Paragraph II, however, is more solidly based and more narrowly drawn. The only advertising claim made by AHP in the category proscribed by Paragraph II(D) of our order was the one noncomparative tension-relief claim for Anacin. Bristol, on the other hand, disseminated at least 20 inadequately substantiated tension-relief claims for Bufferin and Excedrin (slip op. at 44-48) and also claimed without a reasonable basis that Bufferin would cause no stomach upset (slip op. at 30-31). Finally, in contrast to the provision that we entered against AHP, Paragraph II is narrowly limited to internal analgesics—the specific product category for which the offending claims were made. Thus, there is no conflict with the Third Circuit's decision in *AHP*, which, as noted before, sustained a Commission order that taken as a whole was at least as extensive as that here.

Paragraph III-A

Paragraph III-A of our order prohibits Bristol from representing that any nonprescription drug product contains an "unusual" or "special" ingredient when in fact the ingredient is commonly used in other nonprescription drug products that are intended for the same use. Bristol objects that the provision is inappropriate in view of our decision to dismiss the allegations of the complaint that charged the company with falsely representing the uniqueness of the ingredients in Excedrin P.M. See slip op. at 56-57.

Paragraph III-A is not, however, premised on the advertisements for Excedrin P.M. See slip op. at 73. Rather, it was based

on the advertisements for Bufferin and Excedrin that falsely claimed that the analgesic ingredient was something other than aspirin (the violation specifically prohibited by Paragraph IV) and that also implied that those ingredients were special and unusual. See slip op. at 50-52.

Marketplace Changes

Finally, Bristol contends that Paragraph II and III-A should be deleted because it faces the growing market dominance of McNeilab's Tylenol and a significant increase in private enforcement under the Lanham Act, similar state statutes, and through the advertising industry's self-regulatory mechanism.

Under Section 3.55 of the Commission's Rules of Practice the scope of petitions for reconsideration is limited to "new questions raised by the decision or final order upon which the petitioner had no opportunity to argue before the Commission. Bristol, having had adequate opportunity to raise these contentions before the administrative law judge and again on its appeal from the law judge's decision, cannot now assert them for the first time in a petition for reconsideration of our final order.

CONCLUSION

For all the foregoing reasons, the petition for reconsideration is denied in its entirety.

ISSUED: October 14, 1983

Filed: September 28, 1979.

UNITED STATES OF AMERICA

BEFORE FEDERAL TRADE COMMISSION

DOCKET NO. 8917

In the Matter of

BRISTOL-MYERS COMPANY,
a corporation

TED BATES & COMPANY, INC.
a corporation, and

YOUNG & RUBICAM, INC.,
a corporation.

INITIAL DECISION

MONTGOMERY K. HYUN
Administrative Law Judge

September 28, 1979

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UNITED STATES OF AMERICA

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INITIAL DECISION

MONTGOMERY K. HYUN
Administrative Law Judge

W. BENJAMIN FISHEROW, Esq., IRA NERKIN, Esq.; LESLIE R. FAX, Esq.; RANDELL OGG, Esq.
Counsel Supporting the Complaint

GILBERT H. WEIL, Esq., GERALD GUTTMAN, Esq.; BRUCE R. HAFNER, Esq.; LYDIA C. RUSSO, Esq.
WEIL, GUTTMAN & DAVIS
New York, New York
Counsel for Respondent Bristol-Myers Company

GERALD J. BROWN, Esq.
CAHILL GORDON & REINDEL
Washington, D.C.
Counsel for Ted Bates & Company, Inc.

SIDNEY S. ROSDEITCHER, Esq., RONALD W. MEISTER, Esq.
PAUL, WEISS, RIFKIND, WHARTON & GARRISON
New York, New York
Counsel for Young & Rubicam, Inc.

PRELIMINARY STATEMENT

On February 23, 1973, the Federal Trade Commission (''Commission'' or ''FTC'') issued a Complaint charging Bristol-Myers Company (''Bristol-Myers''), Ted Bates & Company, Inc. (''Ted Bates''), and Young & Rubicam, Inc. (''Y&R'') with violations of Sections 5 and 12 of the Federal Trade Commission Act, as amended (15 U.S.C. §§ 45 and 52), in connection with certain advertisements for Bufferin, Excedrin and Excedrin P.M. Similar complaints were issued on the same date against American Home Products Corporation (Docket No. 8918) and Sterling Drug Inc. (Docket No. 8919), in connection with certain advertisements for certain nonprescription or over-the-counter (''OTC'') internal analgesic products marketed by these firms.

On May 7, 1973, Bristol-Myers filed its answer to the Complaint, and on May 9, 1973, Ted Bates and Y&R filed their answers to the Complaint, each denying that it violated Sections 5 or 12 of the amended Federal Trade Commission Act. ALJ William K. Jackson, originally assigned to this proceeding, entered a Prehearing Order, dated March 13, 1974, setting forth the issues of fact and law to govern the case. This case was assigned to me upon Judge Jackson's retirement, effective January 1, 1975. The parties were allowed extensive pretrial discovery. Numerous prehearing conferences were held in order to simplify the issues, to resolve disputes related to discovery and generally to expedite the trial preparation by the parties.

By Order dated February 16, 1977, a joint hearing was ordered with respect to certain common marketing studies and witnesses for the presentation of complaint counsel's cases-in-chief in the three OTC internal analgesic cases (Docket Nos. 8917, 8918 and 8919). Joint evidentiary hearings were held fro. , June 6, 1977 to August 15, 1977. The separate evidentiary hearings for the presentation of complaint counsel's case-in-chief were held from September 5, 1978 to February 21, 1979, after an initial decision in Docket No. 8918 was

filed with the Commission. Respondents' defense hearings began on March 19, 1979 and continued until May 11, 1979. The evidentiary record was closed May 16, 1979.[1] The parties filed simultaneously their proposed findings, supporting memoranda and replies. Some 26 witnesses, most of whom were qualified as expert witnesses, testified. Transcripts of the joint and separate hearings number some 12,400 pages. Over 400 documentary exhibits, including copy tests, marketing studies and medical-scientific studies and analytical tabulations were received in evidence.

The proposed findings, conclusions and orders of the parties and their supporting arguments were carefully considered and to the extent not adopted by this Initial Decision, in the form proposed or in substance, are rejected as not supported by the evidence, irrelevant or immaterial. Any motion appearing on the record and not heretofore or hereby specifically ruled upon either directly or by the necessary effect of the conclusions in this Initial Decision are denied. Upon consideration of the record as a whole and having considered the demeanor of the witnesses, I make the following findings of fact and conclusions of law and order:[2]

---

1 By order dated May 23, 1979, the Commission extended the due date of this Initial Decision to September 28, 1979.

2 For the purposes of this Initial Decision, the following abbreviations were used:

BMF — Bristol-Myers' Proposed Findings.
BMM — Bristol-Myers' Supporting Memorandum.
BRM — Bristol-Myers' Reply Memorandum.
CM — Complaint Counsel's Suporting Memorandum.
CPF — Complaint Counsel's Proposed Findings.
CRM — Complaint Counsel's Reply Memorandum.
F. — Findings in this Initial Decision.
Tr. — Transcripts of hearings, sometimes preceded by the name of the witness.
CX — Complaint counsel's documentary exhibits.
RX, BMRX — Bristol-Myers' documentary exhibits.

FINDINGS OF FACT

I.

Preliminary Findings

1. Bristol-Myers Company (''Bristol-Myers'') is a corporation organized and doing business under and by virtue of the laws of the State of Delaware, with its office and principal place of business located at 345 Park Avenue, New York, New York. Bristol-Myers manufactures, advertises, offers for sale, and sells and distributes certain nonprescription over-the-counter (or OTC) internal analgesic preparations which fall within the classification of ''drug,'' as the term is defined in the Federal Trade Commission Act. The brand-name designations used by Bristol-Myers for three such preparations are ''Bufferin,'' ''Excedrin,'' and ''Excedrin P.M.'' (Answer of Bristol-Myers, Paragraphs 2 and 3).

2. The active ingredients in one tablet of each of the three preparations are as follows:

Bufferin:	aspirin (5 gr.) aluminum glycinate magnesium carbonate
Excedrin:	acetaminophen (1.50 gr.) salicyclamide (2.00 gr.) aspirin (3.00 gr.) caffeine (1.00 gr.)
Excedrin P.M.:	acetaminophen (2.5 gr.) salicylamide (2.00 gr.) aspirin (3.0 gr.) methapyrilene fumarate (25 milligrams)

(Answer of Bristol-Myers, Appendices 1, 2, 3,; CX 925R-U; CX 927B).

Aspirin is a well-known substance widely used in over-the-counter drug products (BMRX 23, 24). Caffeine is a well

known substance widely used in food products and over-the-counter drug products (BMRX 23, 24).

3. In the course and conduct of its business, Bristol-Myers causes Bufferin, Excedrin, and Excedrin P.M. to be transported from its place of business located in various states of the United States to purchasers thereof in various other states and in the District of Columbia. In the course of its business, Bristol-Myers maintains, and at all times mentioned herein has maintained, a substantial course of trade in commerce (Answer of Bristol-Myers, Paragraph 1). From 1971 to 1973 annual consumer sales for Bufferin, Excedrin, and Excedrin P.M. averaged approximately $50 million, $30 million, and $5 million respectively (CX 660A). The average price in 1970 for 100 tablet bottles of Bufferin and Excedrin was $0.99 and $1.01 respectively. The average price in 1970 for an 80 tablet bottle of Excedrin P.M. was $1.30 (CX 661B-D).

4. In the course and conduct of its business, Bristol-Myers has disseminated, and caused the dissemination of, certain advertisements concerning Bufferin, Excedrin, and Excedrin P.M. by the United States mails and by various means of commerce including, but not limited to, advertisements inserted in magazines and newspapers, and in television broadcasts transmitted by television stations located in various states of the United States and the District of Columbia, having sufficient power to carry such broadcasts across state lines, for the purpose of inducing and which were likely to induce, directly or indirectly, the purchase of said drugs, and has disseminated, and caused the dissemination of, advertisements concerning said drugs by various means, including but not limited to the aforesaid medium, for the purpose of inducing and which were likely to induce the purchase of said drugs in commerce (Answer of Bristol-Myers, Paragraph 4). These activities have included the dissemination over a number of years and through various media of the advertising challenged in this matter, including the advertisements in evidence (CX 800; CX 801; CX 802).

5. In promoting these products in advertising from 1960 to 1973 Bristol-Myers expended over $171 million for Bufferin, over $98 million for Excedrin, and over $15 million for Excedrin P.M. (CX 925P, CX 928B). Thus annual advertising expenditures between 1960 and 1973 have averaged approximately $12 million for Bufferin, $7.5 million for Excedrin, and $3 million for Excedrin P.M.

6. According to National Analgesic Market Survey prepared by Young & Rubicam, the advertising agency for Excedrin, the average prescription price at surveyed pharmacies of aspirin in 1971 was $1.08 per hundred tablets. For the same year, the average prescription price per 100 tablets was $2.15 for Bufferin and $2.59 for Excedrin (CX 380Z003, Z001, Y). This survey finding is in accord with our common knowledge and experience which shows one ordinarily expects to pay, and does pay, somewhat higher prices for Bufferin and Excedrin than for plain aspirin at retail stores.

7. Young & Rubicam International Inc., formerly Young & Rubicam, Inc. (''Young & Rubicam'') is a corporation organized, existing and doing business under and by virtue of the laws of the State of New York with its office and place of business located at 285 Madison Avenue, New York, New York (Answer of Young & Rubicam, Paragraph 2).

8. In the conduct of its business at all times mentioned herein, Young & Rubicam has been in substantial competition in commerce, with other corporations, firms, and individuals in the advertising business. Young & Rubicam maintains offices in the commercial centers of the country, including New York City, Detroit, Chicago, Los Angeles and Houston. Among its advertising accounts are some of the largest corporations throughout the United States, including Time, Inc., General Foods, Gulf Oil Corp., and Proctor & Gamble Co. (CX 656).

9. Ted Bates & Company, Inc. (''Bates'') is a corporation organized, existing and doing business under and by virtue of the laws of the State of New York with its principal office and place of business located at 1515 Broadway, New York, New York (Answer of Bates, Paragraph 2).

10. In the conduct of its business at all times mentioned herein, Bates has been in substantial competition in commerce, with other corporations, firms and individuals in the advertising business. Bates maintains offices throughout the world and in New York City to serve national and multi-national corporate clients. Among its clients are The Chase Manhatten Bank, ITT Continental Co., Warner-Lambert Co. and Yardley of London (CX 655).

II.

The Qualifications Of Experts Who Testified In This Proceeding

A. Complaint Counsel's Experts

Dr. Daniel L. Azarnoff

11. Dr. Daniel L. Azarnoff, presently Senior Vice-President, Director of Research and Development, for the three medically related subsidiary companies of G. D. Searle and Company, is an emminent clinical pharmacologist (Azarnoff, Tr. 9159-60; CX 687A).

12. Until recently, Dr. Azarnoff was a Distinguished Professor in the field of Medicine and Pharmacology at Kansas University Medical Center where he served as Director of the University's Clinical Pharmacology-Toxicology Center (Azarnoff, Tr. 9160-61; CX 687A). He has received a number of honorary awards for his outstanding work in medicine and pharmacology, including election as a Markle Scholar in Academic Medicine, election as a Burroughs Wellcome Scholar in Clinical Pharmacology, and designation as a Fulbright Scholar (Azarnoff, Tr. 9165-68; CX 687B).

13. He has served as a consultant to the Food and Drug Administration, specifically a member of the Endocrine Metabolism Advisory Committee. In this capacity, he reviewed foreign therapeutic trials of various drugs to determine if this information should be accepted by the FDA in its evaluation of the safety of these drugs. He has also served as a consultant to

the World Health Organization for the evaluation of drugs in human beings, and is currently serving as Secretary of the Clinical Pharmacology Section of the International Union of Pharmacologists. He has been a member and Vice-Chairman of the AMA Council on Drugs; a consultant to various institutes of the National Institute of Health; and has consulted for several other medical organizations (Azarnoff, Tr. 9165-72; CX 687C).

14. As part of his work as a Distinguished Professor of Medicine and Pharmacology, Dr. Azarnoff teaches medical students, graduate students in pharmacology and practicing physicians. In addition to his extensive teaching commitments, he has also been involved in research activities and in clinical hospital service. His research has involved him in approximately 150 studies, 10 to 15 of which focused on the therapeutic effects of various drugs on human beings. His clinical hospital service has given him the opportunity to work with inpatients and outpatients alike (Azarnoff, Tr. 9162-65, 9174-76).

15. Dr. Azarnoff's clinical research has given him considerable exposure to the various ways of measuring patients' subjective responses. In each of the 10 to 15 therapeutical studies in which he has participated, he has been involved in all phases of the study, ranging from the initial development of the protocol through the execution of the study, and then on through the analysis and interpretation of the data (Azarnoff, Tr. 9164, 9174-75). Dr. Azarnoff has worked with drugs that influence the autonomic nervous system, drugs that influence the central nervous system, drugs that attempt to control angina, and aspirin, among others. In each of these clinical studies, he has been primarily concerned with the elevation of patients' subjective responses to the drugs in question (Azarnoff, Tr. 9164, 9174-75).

16. Dr. Azarnoff is also an editor or advisor to a number of noted American and foreign journals (Azarnoff, Tr. 9170-72; CX 687C). As is evidenced by the evidentiary record and his curriculum vitae, Dr. Azarnoff is highly qualified to provide

expert testimony in the fields of clinical pharmacology, clinical testing of drugs, including analgesics, and the usage of analgesics in the clinical situation.

Dr. William Beaver

17. Dr. William Beaver is presently an Associate Professor of Pharmacology and Anesthesia at the Georgetown University Schools of Medicine and Dentistry and is a recognized expert in the field of analgesics and clinical trials of analgesics (Beaver, Tr. 5896).

18. Dr. Beaver gained extensive expertise in analgesics studies while working as a research associate and then an associate at Memorial Sloan-Kettering Cancer Center with Dr. Raymond Houde between 1963 and 1968. Since 1963, Dr. Beaver has conducted clinical research concerning analgesic drugs, and in 1976 he received a special citation from the Commissioner of the Food and Drug Administration for his advisory work in the area of analgesics and clinical trial design (Beaver, Tr. 5896).

19. Dr. Beaver has written extensively and has published several dozen analgesics studies in medical journals subject to peer review. In addition, he has written chapters in textbooks relating to analgesic drugs (Beaver, Tr. 5897). In 1965, he published in the *American Journal of Medical Science* a comprehensive review of the pharmacology of mild analgesic drugs. That article was based on submissions from manufacturers, including Bristol-Myers, and Dr. Beaver's review of some 1,000 papers on the subject, of which about 490 were directly cited in the review article (Beaver, Tr. 5897-99).

20. Dr. Beaver is one of the leading experts in the field of analgesics and clinical testing of analgesics (Laska, Tr. 10406-07; 10463, 10626; Sunshine, Tr. 9803, 9826-27, 9864).

21. Dr. Beaver served as a member of the Panel on Drugs for Relief of Pain, conceived in 1966 under the auspices of the National Research Council, a subsidiary of the National Academy of Science. The National Academy of Science, chartered by Congress, is an organization whose members are drawn

from among the foremost scientists in the country. The purpose of this group is to provide the government with access to a prestigious group of scientists so as to further the development of science (Beaver, Tr. 5901). Members of the National Research Council are experts in various scientific/technical fields. At the request of the Federal Government, the group will sponsor scientific inquiries where they view such inquiries as appropriate and in the national interest (Beaver, Tr. 5901).

22. Ths FDA, pursuant to various amendments to its enabling act, requested in 1966 that the NAS/NRC carry out an efficacy review of drugs put on the market between 1938 and 1962 (Beaver, Tr. 5900). This responsibility was accepted by the National Research Council. Panels for different subject areas were set up, consisting of six or seven members who were well-recognized experts in particular subject areas (Beaver, Tr. 5902).

23. The Panel on Drugs for the Relief of Pain, of which Dr. Beaver was a member, was given material which had been submitted by drug companies to FDA between 1938 and 1962 for new drug application approval (Beaver, Tr. 5903). This Panel was chaired by Dr. Louis Lasagna, a well-recognized clinical pharmacologist, and it included Dr. Beaver; Dr. Maurice Seevers, who was chairman of the Pharmacology Department at the University of Michigan; Dr. Thomas Kantor of NYU, who was experienced in the evaluation of mild analgesics; Dr. Gravenstein, who was experienced in analgesic research; and Dr. William Martin, who was head of the Drug Addiction Center in Lexington (Beaver, Tr. 5903). The appropriate review panel for each drug was chosen by the central NAS/NRC office on the basis of the indications in its labeling. Materials on specific drugs were then assigned to a panel member based on his expertise and workload (Beaver, Tr. 5904). Dr. Beaver served as co-primary reviewer for Bufferin submissions (Beaver, Tr. 5910). The primary reviewer then considered the drug company data along with the archival literature, which included published and unpublished studies. New issues of safety were considered as were certain claims,

e.g., superiority, in light of any new information. A preliminary review was prepared and circulated to the entire Panel (Beaver, Tr. 5905). A final report was prepared by the Panel as a whole. Final editing was done by the NAS/NRC central office (Beaver, Tr. 5906). The final approval prior to release to FDA was then secured from the Panel chairman.

24. Bufferin was among the drugs considered by the Panel since it was granted a New Drug Application ("NDA") between 1938 and 1962. Bristol-Myers was asked to submit literature references with respect to indications in labeling, but initially did not submit any literature references (Beaver, Tr. 5907-08). Because the Panel believed that certain Bufferin claims in labeling went beyond accepted indications for aspirin, another letter was sent to Bristol-Myers requesting substantiation for claims addressing speed of onset of action, lack of gastrointestinal side effects and tension relief. In response, Bristol-Myers submitted reprints of published articles and certain in-house, unpublished blood level studies dealing primarily with the pharmacokinetics of Bufferin compared to other aspirin. These materials and the published literature were reviewed by Dr. Beaver and Dr. Seevers, the co-primary reviewer. Bristol-Myers was only required to submit evidence that supported its claims for Bufferin, rather than all pertinent data relating to a particular indication, whether favorable or not (Beaver, Tr. 5909-11).

25. A draft report was prepared by Drs. Beaver and Seevers and was submitted for the approval of the entire Panel (Beaver, Tr. 5911-13). When the final report was approved after editing, it was turned over to the NAS/NRC and forwarded to FDA (Beaver, Tr. 5915).

26. Based on these reports, FDA set up a Drug Efficacy Study Implementation (DESI) group to address what should be done with respect to the issues raised in the various reports, such as CX 511 (Beaver, Tr. 5916). The Panel's evaluation (CX 511) was published in the *Federal Register* (Beaver, Tr. 5917-19) and a copy was sent to Bristol-Myers (Beaver, Tr. 5919).

Dr. Byron William Brown

27. Dr. Byron Brown holds a Ph.D. degree in biostatistics from the University of Minnesota. Currently he is Professor and Head of Biostatistis at Stanford University (Brown, Tr. 4843- 45; CX 694). Dr. Brown is involved in academic duties and is consulting with research investigators, the Federal Government and pharmaceutical manufacturers in problems involving research in biology and medicine (Brown, Tr. 4845).

28. Dr. Brown's primary interests center on the application of biostatistics to biological assays and related clinical trials. However, his statistical consultancies involve him in joining efforts with investigators in other fields of biology and medicine (Brown, Tr. 4846). For example, Dr. Brown is a consultant to the National Academy of Sciences, the National Cancer Institute, the American Heart Association, the National Aeronautics and Space Administration, the University Group Diabetes Project, the Food and Drug Administration, the Institute for Nutrition for Central America and Panama, as well as numerous other organizations, committees and associations (CX 694B).

29. Approximately one-quarter to one-half of Dr. Brown's publications (CX 694C-H) deal with the evaluations of drugs, including some specifically devoted to the evaluation of analgesics (Brown, Tr. 4846-47).

30. Dr. Brown is one of the leading experts in biostatistics, including the applications of that discipline to the design and analysis of clinical trials of analgesics and other drugs.

Dr. Frederick Evans

31. Dr. Frederick J. Evans is Senior Research Psychologist in the Unit for Experimental Psychiatry, Institute of Pennsylvania Hospital. He is also an associate professor of psychology at the University of Pennsylvania. He was a Fulbright Scholar, and conducted research at the Harvard Medical School (Evans, Tr. 6311-14). Dr. Evans is a highly experienced researcher in the psychology of pain and pain control and subjective response methodology (Evans, Tr. 6313-17). He is a

member of the board of the American Pain Society, a member of the executive committee of the eastern chapter of the International Association for the Study of Pain, and is associate editor of the *International Journal of Clinical and Experimental Hypnosis* (Evans, Tr. 6318; CX 692A-D). He has served on a number of peer review groups evaluating pain studies for the United States and Canadian governments, as well as for numerous learned journals (Evans, Tr. 6318). He has also served as a consultant on and reviewer of grants and studies involving analgesic testing (Evans, Tr. 6335). He has published widely in the field of subjective response methodology (CX 692G-O).

32. The Unit for Experimental Psychiatry with which Dr. Evans is associated concerns itself with laboratory research into problems of mental health and human suffering. The research is concentrated on the interrelationships between subjective processes (*i.e.*, subjective response) and observable behavior in the laboratory, and the evaluation of subjective behavior such as pain and placebo response (Evans, Tr. 6314). To these ends, Dr. Evans devotes approximately one-fourth of his full-time research employing several different models of experimental pain (Evans, Tr. 6334). Dr. Evans' laboratory is also well known for its research into the methodological problems of generalizing laboratory study findings to the clinical situation (Evans, Tr. 6325).

33. By his background, training and experience, Dr. Evans is well qualified to speak to issues of pain and its response to treatment, the psychological factors and experimental pain methodology.

Dr. Richard S. Farr

34. Dr. Richard S. Farr is Chairman of the Department of Medicine of the National Jewish Hospital in Denver. Dr. Farr, who is widely recognized as a preeminent researcher in immunology, has had extensive clinical training in the diagnosis and management of bronchial asthma and allergy, including the asthma and allergic effects of aspirin. He previously headed the allergy/immunology sections at the University of Pitts-

burgh and the Scripps Clinic in La Jolla, California, and is also known for the development of the so-called Farr test, which is still widely used in immunology research (Farr, Tr. 2541-50).

35. Dr. Farr has been deeply involved in the clinical study of aspirin side effects since 1969 and is responsible for the development of the aspirin challenge procedure originating at National Jewish Hospital (Farr, Tr. 2553-60).

36. Dr. Farr has had extensive experience in the design, execution and analysis of clinical tests of the side effects of aspirin and has published widely on the topic. His experience extends to the clinical management of asthmatic and allergic patients and he has widely lectured and taught on this topic (Farr, Tr. 2558-60).

37. Dr. Farr served as the president of the American Academy of Allergy and has been associated with many other professional associations with particular interest in asthma and allergy. Dr. Farr is also a Distinguished Service Professor of the University of Chicago and is the recipient of the Borden Award for his outstanding work in the area of immunology (Farr, Tr. 2541-62).

38. Dr. Farr is a leading expert in the fields of asthma and allergy in general and the asthmatic and allergic effects of aspirin and aspirin-containing drugs in particular.

Dr. William H. Forrest

39. Dr. William H. Forrest is an Associate Professor of Anesthesiology at Stanford University. He is a recognized expert in the field of analgesic testing and has had extensive experience evaluating analgesics. In fact, he has spent half of his time supervising, performing, or evaluating clinical research on analgesics (Forrest, Tr. 8848-49; 8860-63; 8869-71; 8875).

40. Dr. Forrest has had extensive experience working with and developing subjective response methodologies. His introduction to clinical research came while he was a research fellow at Stanford in 1962. During this year, he worked under Dr. J. W. Bellville, a respected researcher in the field of analgesic

evaluations and Chairman of the FDA Analgesics Panel until he died (Forrest, Tr. 8850-51).

41. Dr. Forrest later became Chairman of the Veterans Administration Cooperative Analgesic Study. In the landmark Cooperative Study, analgesics were evaluated using a subjective response methodology in five to seven different Veterans Administration hospitals located in various parts of the country. The results of the Cooperative Study demonstrated that carefully trained and supervised nurses and researchers could perform the same work in several different settings and obtain sound data relating to the efficacy and relative potency of a variety of intra-muscular and orally administered analgesics. The Cooperative Study spanned a 14-year period and involved over 100 clinical analgesic studies (Forrest, Tr. 8854-56; 8858-59; 8864-65; 8872-73; 8876-81; CX 678A-B).

42. During the last 14 years, Dr. Forrest has also been actively involved in various capacities with the National Research Council of the National Academy of Sciences (Forrest, Tr. 8856-57). He was involved in the 1960's in the planning phases of the National Halothane Study sponsored by the Council (Forrest, Tr. 8852). He has acted as a consultant to the Council on Anesthesia; and attended annual meetings sponsored by the Council for researchers working in the field of analgesics. At these meetings, Dr. Forrest has also presented numerous papers in the field (Forrest, Tr. 8856-57; 8865-67; CX 678B). In addition, he has published over 60 articles dealing with analgesics, clinical testing, and the subjective response methodology (Forrest, Tr. 8860-63; CX 678D-I).

43. Dr. Forrest is an eminent expert in the fields of clinical testing of analgesics, the subjective response methodology, and the efficacies, comparative efficacies, and side effects of various analgesics.

Dr. Morton Grossman

44. Dr. Morton Grossman, Chief of the Gastroenterology Section of the Veterans Administration Wadsworth Hospital in Los Angeles, is recognized as one of the preeminent research-

ers and practitioners of gastroenterology in the world. Dr. Grossman, who currently directs the Center for Ulcer Research and Education in Los Angeles, is one of six Senior Medical Investigators in the Veterans Administration, and has been Chief of the Gastrointestinal Section at the Veterans Administration Hospital in Los Angeles. Dr. Grossman is also a professor of medicine and physiology at the University of California at Los Angeles, has taught at major medical schools throughout the country and has served as a member of or advisor to many distinguished professional groups, including the National Academy of Science, National Research Panel on Gastrointestinal Drugs, the FDA's OTC Panel on Antacids and the Gastrointestinal Drug Advisory Committee of the FDA (Grossman, Tr. 7789-93).

45. Dr. Grossman's experience includes years of clinical practice with patients suffering gastrointestinal diseases, as well as considerable research in the areas of physiology and gastroenterology. In this regard, Dr. Grossman has done research on the mechanism and effects of aspirin ingestion on the gastrointestinal track and has published many articles on this topic in learned journals. Dr. Grossman has also served on various editorial boards of scientific journals, such as the *American Journal of Physiology*, and currently chairs the editorial board of *Gastroenterology*, the official journal of the American Gastroenterological Association. Dr. Grossman has published over 350 articles in journals, contributed to scores of textbooks and other resource works on gastroenterology (Grossman, Tr. 7792-96).

46. Dr. Grossman has also been the recipient of major awards and honors in his field, including the Freeden-Wald medal of the American Gastroenterological Association, which is its highest award. He also has held high offices with many of the professional societies concerned with problems of gastroenterology (Grossman, Tr. 7796-97).

47. Based on his education and training, as well as his wealth of research and clinical experience, Dr. Grossman is eminently qualified to speak to gastroenterology generally and

specifically to gastrointestinal effects of aspirin and aspirin containing products, as well as the effect of buffers in such products.

Dr. Charles G. Moertel

48. Dr. Charles G. Moertel, who presently serves as the Director of the Mayo Clinic's Comprehensive Cancer Center, Chairman of its Department of Oncology, and Professor of Medicine at the Mayo Medical School, is an expert in evaluating patients' subjective responses to analgesics and is preeminent in the field of clinical testing of drugs (Moertel, Tr. 5515;CX 680A). Dr. Moertel's expertise in the analysis of patients' subjective responses to various kinds of drugs, including analgesics, has been developed over the last 24 years through his clinical and research activities at the Mayo Clinic (Moertel, Tr. 5520-23).

49. At the Mayo Clinic, Dr. Moertel is involved in the evaluation of therapeutic agents. His involvement covers all of the Clinic's treatment programs designed to deal with malignant diseases starting in the gastrointestinal tract. He has done a great deal of work over an extended period of time in the evaluation of symptomatic and supportive care of the cancer patient, and this involvement has encompassed the evaluation of analgesic agents, anti-emetic agents, and diuretic agents (Moertel, Tr. 5517, 5520-22).

50. Dr. Moertel's work with analgesics evolved from the primary need of his advanced cancer patients to have effective treatment for pain. Since the predominent part of his practice was to treat patients whose conditions had advanced beyond a point where surgery could help, but who suffered from mild to severe pain, Dr. Moertel developed an interest in the comparative efficacies of the available analgesics. He conducted two studies involving numerous OTC and prescription oral analgesics to determine their comparative efficacies in relieving pain. Both of these studies were published in leading medical journals subject to peer review (Moertel, Tr. 5521-22; CX 680J, N).

51. In addition to these two studies, Dr. Moertel has evaluated some of the newer chemical agents developed by pharmaceutical companies for analgesics purposes (Moertel, Tr. 5522). He has conducted a number of clinical studies using antiemetic and chemotherapeutic drugs as well (Moertel, Tr. 5522). In all of these studies, Dr. Moertel has been involved in the analysis and evaluation of patients' subjective responses (Moertel, Tr. 5523).

52. In addition to contributing articles dealing with specific research studies, Dr. Moertel has also submitted articles for publication which have dealt with analgesics in a broader sense and have utilized his overall clinical experience in the management of cancer pain. These articles have appeared in several textbooks of which he has been the primary author, or in which he was invited by the primary author to contribute (CX 680E, F, G, J, K). Dr. Moertel is a member of the Editorial Board of the *Journal on Cancer*, and he is an Associate Editor of *Cancer Medicine*, a standard textbook in medical oncology (Moertel, Tr. 5518).

53. As a practicing physician, Dr. Moertel prescribes, administers, and advises patients on a daily basis in the usage of analgesics. In his practice he has had occasion to prescribe aspirin in these clinical situations (Moertel, Tr. 5523).

54. Dr. Moertel was appointed by the FDA to its Oncologic Drugs Advisory Committee. As a member of this Committee, he advises the FDA on clinical protocols for new drugs for use in the treatment of cancer patients. Dr. Moertel also serves on the Phase One Study Group of the National Cancer Institute. In this capacity, he helps to evaluate the types of protocols that will be most appropriate to determine the clinical value of new agents for the treatment of malignant diseases (Moertel, Tr. 5518-20). For all of these reasons, Dr. Moertel is eminently qualified to present expert testimony concerning clinical tests, the evaluation of patients' subjective responses, and the clinical testing of analgesics.

Dr. Karl Rickels

55. Dr. Karl Rickels is Professor of Psychiatry and Pharmacology at the University of Pennsylvania. Dr. Rickels is an eminent practitioner in the diagnosis and management of patients exhibiting nonpsychotic symptoms, such as anxiety and tension. Dr. Rickels also directs the Private Practice Research Group, funded by NIH, which is the only unit in the country conducting a large scale research with private patients of family physicians who suffer tension and stress (Rickels, Tr. 6489-91).

56. Dr. Rickels, Director of the Psychopharmacology Research Unit of the University of Pennsylvania since 1962, was recently appointed to an endowed chair in Human Behavior. He has also widely lectured and consulted both with industry and academics in the area of psychopharmacology and currently sits with the Clinical Pharmacology Study Session of the National Institute of Mental Health. Dr. Rickels has had extensive experience in the design, execution and review of clinical tests of drugs, including aspirin, for tension relief and has often consulted with industry on the development of protocols for such clinical tests (Rickels, Tr. 6495, 6499-6502).

57. For three years, Dr. Rickels chaired FDA's OTC panel on Nighttime Sleep-Aids, Daytime Sedative and Stimulants, and he has published widely on psychopharmacology topics including the effects of aspirin on tension relief (Rickels, Tr. 6492-95; 6501-02).

58. Based on his background, training, and experience, Dr. Rickels is an eminent expert well qualified to speak to psychopharmacology and tension and particularly to the effects of aspirin and caffeine on tension.

Dr. Eugene Smith

59. Dr. Eugene Smith is a psychologist at the Massachusetts General Hospital in the Department of Anesthesia and Psychiatry. He is also an associate professor of psychology at the Harvard Medical School. Dr. Smith holds a Ph.D. degree from the University of Rochester. Dr. Smith has been continu-

ously associated with Harvard and the Massachusetts General Hospital since 1954 (Smith, Tr. 5387-88). His work has concentrated in the effects of drugs on mood, physical and mental performance; and he has done a large number of studies in pain and subjective responses to pain. Much of his work has been in the area of experimentally induced pain. However, he has done a number of subjective response studies investigating the activity of analgesics in post-partum and post-operative pain (Smith, Tr. 5388-89). Dr. Smith is a member of numerous professional associations, and most of his studies have been funded by agencies of the U.S. Public Health Service or the National Institutes of Health (Smith, Tr. 5389-90).

Dr. Donald D. Stevenson

60. Donald D. Stevenson, M.D., is a member of the allergy/immunology division at the Scripps Clinic at La Jolla, California. Dr. Stevsnson, who also has a clinical appointment in the Department of Internal Medicine at the University of California, has extensive experience in the clinical diagnosis and management of patients suffering from various allergies and asthmatic conditions, including those associated with aspirin. He has designed and conducted clinical tests of drugs to determine their safety and effectiveness in treating asthmatic and allergic conditions and has conducted clinical tests and controlled challenges in order to determine the asthmatic and allergic effects of aspirin ingestion.

61. Dr. Stevenson has lectured and taught generally on the subject of immunology and particularly on the asthmatic and allergic effects of aspirin ingestion. He has published articles and studies relating to these topics and is familiar with the literature and current thinking regarding aspirin side effects.

62. Dr. Stevenson is associated with various scientific and medical groups, including the American Academy of Allergy and the West Coast Allergy Society, with primary interest in asthma and allergy, and has participated in meetings and conferences held by such organizations (Stevenson, Tr. 1454-71). Based on his background, training and experience, Dr. Stevenson is highly qualified to speak to immunology, asthma

and allergy generally and specifically to the asthmatic and allergic side effects of aspirin and aspirin-containing products.

Dr. Timothy Brock

63. Dr. Timothy C. Brock is Professor of Psychology at Ohio State University and is a licensed psychologist. Dr. Brock holds a Ph.D. degree from Yale University in psychology, with a specialization in social psychology. In 1955 he joined the Yale Communication and Attitude Change Program and began a career in the field of persuasion and communication studies, and has had extensive experience in evaluating the formation, reinforcement and endurance of beliefs and attitudes. This experience includes conducting and evaluating research in this area, including the formation of attitudes about consumer goods and services (Brock, Tr. 8537-40; 8549-53; CX 826B-H). Dr. Brock has extensively contributed since 1957 to the body of literature regarding the role of communication in attitude formation and change. His numerous publications encompass research and analyses of persuasion techniques, measurement of attitude change, and identification of public opinion and attitudes (CX 826B-H), including a number of studies regarding beliefs and attitudes about consumer products, such as small toys, food, paint, and cigarettes (Brock, Tr. 8554-56, 8559-61). Dr. Brock's research has also included studies on the endurance of people's beliefs and attitudes (Brock, Tr. 8567-68). The research methodology employed by Dr. Brock has been substantially similar to that employed by the marketing community (Brock, Tr. 8565-66). Dr. Brock has also performed two studies that address the role of persuasive communications on consumers' perceptions of the performance of drugs. That research showed that advertising, like communications, had a direct effect on the desire to self-medicate, and that consumers' beliefs about drugs were heavily influenced by the information they received regarding their performance (Brock, Tr. 8559-61). Dr. Brock has also served on the editorial boards of several professional journals and has frequently reviewed articles relating to the formation

and persistence of attitudes submitted for publication to a number of other professional journals. The research includes work in the fields of belief formation and change, the measurement of beliefs and attitudes, and the effectiveness of various types of communication to induce attitude change (Brock, Tr. 8545-47).

64. Dr. Brock is a member of numerous professional associations in the fields of psychology and consumer psychology including the American Psychological Association, the American Sociological Association, the Society of Experimental Social Psychology and the American Association for the Advancement of Science. He has been elected by his colleagues to Fellowship status in the American Psychological Association, the American Sociological Association and the American Association for the Advancement of Science as recognition of his professional contributions (Brock, Tr. 8544). Recently, Dr. Brock was invited by the American Psychological Association to deliver a paper entitled "Designs for Corrective Advertising" (Brock, Tr. 8653). He was also elected Secretary-Treasurer of the Evaluation Research Society, a national society of professionals concerned with the measurement and assessment of the long-term effects of various social and educational programs (Brock, Tr. 8541).

65. Dr. Brock is a highly qualified expert in social psychology, with special expertise in the techniques and effects of persuasion on the source and duration of consumer beliefs and attitudes. He is also qualified as an expert in analyzing the role of communications as a source of consumer attitudes and beliefs and as an expert in the design and analysis of research that assesses the source, nature, and endurance of consumer attitudes and beliefs.

Dr. Ivan Ross

66. Dr. Ivan Ross is a Professor of Marketing at the University of Minnesota, College of Business Administration, and is a licensed consulting psychologist. Dr. Ross has had extensive training and experience in the fields of consumer psychology and behavior and marketing and marketing research (CX 699;

Ross, Tr. 6907-20, 6926-38). This has included extensive training and experience in evaluating advertising and the effects of advertising over time on consumers and upon their attitudes and beliefs. It has also included extensive training and experience in conducting and interpreting research in these areas. Dr. Ross is familiar with the literature in these areas. In addition to his academic training (Ross, Tr. 6908) and work in the areas of advertising and promotion, consumer behavior, marketing and marketing research (Ross, Tr. 6909-12; 6914-15), Dr. Ross has had extensive experience working with advertisers and advertising agencies on advertising content and strategy for a variety of consumer goods and services and with various consumer research techniques, such as focus groups, copy tests, penetration studies, and image studies (Ross, Tr. 6913-14, 6916-18, 6927-29). Dr. Ross has also been a consultant with the Food and Drug Administration's Bureau of Foods (Ross, Tr. 6926).

67. Dr. Ross is a member of a number of professional associations in the areas of psychology, marketing, advertising, and consumer research (Ross, Tr. 6929, 6933) and has held both elected and appointed positions in these organizations (Ross, Tr. 6929, 6933). He has also served as an editor and reviewer of articles and papers in consumer behavior and advertising research for journal publication and presentation before various professional organizations (Ross, Tr. 6933). Dr. Ross has presented papers before professional organizations in the areas of marketing, consumer research, and psychology, and his articles, studies, and other writings in fields such as consumer beliefs, consumer behavior, and advertising have been published in peer-reviewed journals and other publications (Ross, Tr. 6933-35; CX 699). His model for studying techniques of advertising evaluation has been cited by a leading textbook in advertising, and he is currently writing textbooks on marketing and advertising (Ross, Tr. 6933-35). Dr. Ross has been chosen to arbitrate complaints about advertising for the Minnesota Advertising Review Board and to mediate consumer complaints for the Better Business Bureau of Min-

nesota (Ross, Tr. 6930-32). Finally, he has appeared as an expert witness in a number of FTC cases and his testimony involved both the conduct and evaluation of consumer research (Ross, Tr. 6926, 6928).

68. Dr. Ross' training, professional experience, and familiarity with the literature qualify him as an expert in psychology, specializing in consumer psychology and consumer behavior, marketing, and marketing research. He has a broad background in evaluating advertising, including the effects of advertising on consumers and on their attitudes and beliefs, as well as in the conduct and interpretation of advertising and consumer research (CX 699; Tr. 6907-20, 6926-38).

B. Respondents' Experts

Dr. Abraham L. Sunshine

69. Dr. Abraham L. Sunshine is a practicing physician specializing in internal medicine and clinical pharmacology. Dr. Sunshine received his undergraduate training and a masters degree at University of Wisconsin and attended and received an M.D. degree from the Temple University School of Medicine in 1953. He has held a National Institute of Health Research Fellowship in immunology at the University of Wisconsin and was an intern and resident of Bellevue Hospital in New York City. Dr. Sunshine was an instructor in medicine at the NYC College of Medicine and, while on active duty with the USAF, was Chief of the Cardiovascular Section and Chief of the Department of Medicine at Clarks Air Force Base in California and Director of Out-Patient Services at Travis Air Force Base.

70. Dr Sunshine holds a diploma from the American Board of Internal Medicine, is a Fellow of the New York Academy of Medicine, The American College of Physicians, and is a member of the New York County and American Medical Associations, The New York Heart Association, The American Federation for Clinical Research, The American College of Clinical Pharmacology and Chemotherapy, The New York Academy of Sciences and the International Association of the

Study of Pain. In addition, Dr. Sunshine has been appointed Chairman of the Analgesic Section of the American Society for Clinical Pharmacology and Therapeutics, which publishes the *Journal of Clinical Pharmacology and Therapeutics*.

71. Dr. Sunshine is a Professor of Clinical Medicine at New York University Medical Center and is an attending physician at the Arthur C. Logan Memorial Hospital, Bellevue Hospital and New York University Hospital. Dr. Sunshine has published extensively in the area of clinical pharmacology and therapeutics and the methodology of subjective response clinical studies (Tr. 9592-95; BMRX 38).

72. Dr. Sunshine has been studying subjective response research methodology, particularly in relation to analgesic, hypnotic and sedative drugs for the past 19 years. Dr. Forrest, one of complaint counsel's witnesses, recognized Dr. Sunshine as a "very, very able investigator in the field of analgesics." (Tr. 9596).

73. Dr. Sunshine's research has been conducted at Knickerbocker Hospital, Bellevue Hospital (part of New York University Medical Center), Philadelphia General Hospital, The University of Puerto Rico, The University Hospital and The Maternity Hospital in Caracas, Venezuela, and his own office in New York City (Tr. 9597).

74. Dr. Sunshine held a National Institute Health Grant to study pain and the influence of aspirin on pain as well as the methodology of investigating those phenomena (Tr. 9598). Much of the work done by Dr. Sunshine and Dr. Laska has since been emulated by other researchers in the field. Dr. Forrest's opinions of Drs. Sunshine and Laska would be shared by his peers (Tr. 9017).

75. Dr. Sunshine has consulted with and done research for most of the major drug companies in the United States including Sterling Drug, Eli Lilly & Co., Pfizer, Merck, McNeil, Warner-Lambert and Parke Davis (Tr. 9599-9600).

76. Some of the companies for which Dr. Sunshine consulted market products in competition with those of Bristol-Myers (Tr. 9600).

77. Dr. Sunshine qualified as an expert in internal medicine, clinical pharmacology and the conduct of subjective response tests of oral analgesic products (Tr. 9647).

Dr. Eugene M. Laska

78. Dr. Eugene M. Laska is Deputy Director for Research and Development of the Rockland Research Institute and is a mathematician practicing in the field of mathematical statistics. In the course of his duties, he directs the Information Sciences Division of the Rockland Research Institute that deals with the computer developments in the fields of health and mental health. Dr. Laska has been involved in the last 12 years in developing information systems for use in health research in health-related matters including one system that deals specifically with research in mathematical statistical models for the analysis of data resulting from clinical trials (Tr.10145). Dr. Laska has also recently been appointed Research Professor in the Department of Psychiatry at the New York University Medical School (Tr. 10146).

79. Dr. Laska has, from May 1974 through May 1976, been the American Statistical Association representative to the American Association for the Advancement of Science section on medical science (Tr. 10149).

80. Dr. Laska was, from 1972 to 1976, a member of the Computer and Biomathematical Science Section of the National Institutes of Health (Tr. 10150-51). In his capacity as a member of that section, Dr. Laska reviewed grant applications for possible NIH funding.

81. Dr. Laska has been a consultant to many drug manufacturers and has also been closely associated with a number of investigators conducting clinical trials in analgesics including Dr. Abraham Sunshine and Dr. Thomas Kantor (Tr. 10151-52).

82. Dr. Laska has frequently met with the Research Committee on drug addiction headed by Dr. Nathan Eddy and attended meetings of the Association of Clinical Pharmacology and Therapeutics that is chaired by Dr. Abraham Sunshine, giving a paper recently at the Association of Clinical Pharmacology and Therapeutics (Tr. 10154).

83. Dr. Laska also was a consultant to the Veterans Administration Cooperative Program on analgesic testing headed by Dr. William Forrest. Dr. Forrest acknowledged Dr. Laska as "a very excellent biostatistician who has spent a good portion of his time, if not the major portion of it, in this whole problem of bioassay of analgesics." (Tr. 10155).

84. Dr. Laska has met with such clinical researchers as Dr. Raymond Houde, Mr. Stanbley Wallenstein, Dr. William Beaver and others (Tr. 10155).

85. In the course of his work with statistics and biostatistics involved in bioassay studies, Dr. Laska is intimately involved in the design of those experiments. His participation included the formulation of the way in which the observer asked questions, the kind of information to be elicited, the assumptions to be made in the analysis of data, the kind of information to be collected (Tr. 10157-59).

86. Dr. Laska testified that he participated in approximately 100 subjective response studies including head-to-head studies in the fields of sleep and psychiatric evaluation. In addition, he has read hundreds of articles on analgesic research and methodology, including head-to-head trials (Tr. 10160).

87. Dr. Laska was qualified as an expert in comparative testing of analgesic drugs (Tr. 10166; BMRX 7).

Dr. Ben Marr Lanman

88. Dr. Lanman is Vice President and Medical Director of the Bristol-Myers Products Division and has been employed by Bristol-Myers since 1962. He received his M.D. degree from the Jefferson Medical School in Philadelphia, Pennsylvania, was an intern at Jefferson Hospital and a resident in surgery and thoracic surgery at the Columbia Presbyterian Medical Center, Columbia University and Bellevue Hospital in New York. From 1953 to 1962, Dr. Lanman was Medical Director of Shenley Industries dealing with primarily prescription drugs (Tr. 11404-07). As Medical Director of Bristol-Myers Products, Dr. Lanman is responsible for all medical aspects of products sold by the division including testing for efficacy, safety and advertising substantiation (Tr. 11407-08).

89. Dr. Lanman and the other members of the Bristol-Myers Products Medical Department keep current with the medical literature insofar as it relates to and concerns the products manufactured by the Products Division (Tr. 11409-10). Dr. Lanman and the other members of the Medical Department of the Products Division attend meetings of the American Society of Clinical Pharmacology and Therapeutics, the meetings of the committee on Drug Dependence of the National Research Council, The American Pain Association, The Eastern Pain Association, The American Association for the Study of Headache. Dr. Lanman has presented a paper at a meeting of the American Association of Clinical Pharmacology and Therapeutics (Tr. 11411-13). Dr. Lanman regularly meets with independent outside clinical researchers. For example, Bristol-Myers Products co-sponsored and Dr. Lanman co-chaired a symposium on pain in 1964 or 1965 at which the outstanding experts in the analgesic field, including Drs. Sunshine, Laska, Kantor, Belleville, Forrest, Houde, Brown, Beaver and Wallenstein, participated (Tr. 11414-15).

90. In the course of his discussions with the investigators who worked for Bristol-Myers, some of whom are well-known and well respected in the field, Dr. Lanman contributes to the design and methodologies to be used in conducting those researches for Bristol-Myers (Tr. 11416-17), although Dr. Lanman has not participated in any clinical study.

91. Dr. Lanman has been qualified as an expert in the study and research methodologies used to investigate analgesic drugs and their activities (Tr. 11420-21; 11427; BMRX 1).

Dr. Walter B. Elvers

92. Dr. Walter B. Elvers is Associate Medical Director of Bristol-Myers Products, a division of the Bristol-Myers Company (Tr. 10745). Dr. Elvers obtained his bachelor's degree at Columbia Unversity, and was awarded the DDS degree and attended post-doctoral training in orthodontics at Columbia University Dental School (Tr. 10746). Dr. Elvers served two

years in the Army Dental Corps and was in private practice in orthodontics for several years prior to joining Bristol-Myers (Tr. 10746).

93. His principal duties at Bristol-Myers were to initiate studies, to suggest and negotiate the design features of them, to supervise the study in progress and interpret the results of the studies at their conclusions (Tr. 10747-48). Dr. Elvers is familiar with and has kept current with the design and methodologies involved for clinical and experimental studies (Tr. 10752-53). Dr. Elvers has been involved with (and has had primary or supervisory responsibility for) over 2,500 studies in the past 20 years. The vast majority of this work is in clinical rather than experimental research (Tr. 10748-49). Over 275 of the studies in which Dr. Elvers has been involved concerned analgesics and approximately 170 were clinical studies (Tr. 10749-50). However, Dr. Elvers himself has not conducted any analgesic study, or other clinical study of drugs.

94. Dr. Elvers was qualified as an expert in the design, conduct and analysis of clinical tests of analgesics (Tr. 10754; BMRX 2).

Dr. Jacob Jacoby

95. Dr. Jacob Jacoby is a Professor in the Psychological Sciences Department at Purdue Univesity, where he heads the Consumer Psychology Program which is widely known for its innovative and extensive work regarding the application of the science of psychology to the study of consumer behavior. In addition to his teaching, Dr. Jacoby has done extensive empirical research and has published numerous articles dealing with consumer decision making and behavior and the effects of various factors, including advertising, upon consumers (Tr. 9484-9513).

III.

The Market Research And Other Documentary Exhibits Offered By Complaint Counsel Are Reliable

A. Image and Advertising Penetration Studies

1. *CX 346: The Assets and Liabilities Study (1967)*

96. The 1967 "Assets and Liabilities Study of Adult Analgesics" (CX 346) was designed by Dancer-Fitzgerald-Sample, Inc., and executed by Crossley Surveys for Sterling Drug, Inc., the manufacturer and marketer of Bayer brand aspirin. Its stated purpose was to "provide assets and liability profiles for Bayer Aspirin and other leading brands of analgesics products," and to "serve as a 'benchmark' against which data from future assets and liabilities studies may be measured" (CX 346C; Miller, Tr. 209-10). It is a replication of an earlier study that Crossley Surveys had done for Dancer-Fitzgerald-Sample (hereinafter "DFS") (Leonard, Tr. 88-89).

97. The survey of households through personal interviews was designed and executed by highly experienced individuals and companies. Dancer-Fitzgerald-Sample, Inc. is a major national advertising agency. It held the Bayer Aspirin account of Sterling Drug, Inc. at the time the study was performed. DFS designed many consumer research studies for its clients, who included General Mills, Hanes and CPC (Miller, Tr. 208-09). Lloyd C. Miller, who designed CX 346, was and is Vice-President and Associate Director for Research of DFS. Mr. Miller testified concerning the design and analysis of the study. He had held his position with DFS for 13 years at the time of his testimony. His academic background includes a Bachelor's degree in Business Administration from City College of New York and an MBA from New York University. He had been involved in conducting all types of marketing research for over 16 years at the time of the 1967 study (Miller, Tr. 206-07).

98. Crossley Surveys, Inc. has over 50 years' experience in sample survey research for all types of clients, including manufacturers, media, government, and advertising agencies. It has conducted attitude studies, new product research, media research and public opinion research for a variety of clients including Gillette, General Foods, American Oil and Texaco (Leonard, Tr. 86-87).

99. Franklin B. Leonard, who personally supervised the execution of the 1967 Assets and Liabilities Study, is President of Crossley Surveys, and has been employed at the company for 26 years. He holds a B.S. degree in Industrial Engineering from Yale University, and since has held positions at Crossley ranging from trainee to project director (Leonard, Tr. 83-87).

100. The sample for this study was a "multi-stage stratified area sample. The sample design provides for the selection of individual respondents by dividing the country as a whole into smaller and smaller units, from major markets to minor civil divisions to blocks, and from blocks to households. "Stratification" refers to that control designed to insure that the samples fairly represented diverse demographic attributes of the population as a whole. Such stratification related to sex (that it was half men and half women), and to geography. The sample was designed to be representative of the U.S. population in terms of the proportional representation of the four geographical regions, three sizes of standard metropolitan statistical areas and one size of nonmetropolitan counties in the U.S. (Leonard, Tr. 95-96). Thirty-five primary units, or markets, were selected from a national probability sampling frame of 80 primary sampling units to be representative of the whole United States. Within those 35 markets, Crossley Surveys selected minor civil divisions in proportion to their relative population (Leonard, Tr, 97-98). Within individual divisions, urban block clusters were selected systematically from census block statistics whenever that was possible. Once a particular block was selected, a random technique was used to designate a starting point on the block for interviewers to commence their interviewing. From that starting point, interviewers were

given explicit instructions on which houses to contact (CX 1007). These instructions left no discretion in the hands of the interviewer (Leonard, Tr. 100).

101. The sampling procedure outlined above is consistently used by Crossley Surveys. It yields results upon which marketing decisions are made (Leonard, Tr. 102-05). The procedure was discussed with, and explicitly approved by, Dancer-Fitzgerald-Sample, Inc. (Leonard, Tr. 102).

102. The 1967 "Assets and Liabilities Study" was executed according to Crossley Surveys' normal survey procedures. Most of the field work supervisors and interviewers on the project were people with whom Crossley Surveys had had substantial favorable experience (Leonard, Tr. 107). All interviewers were personally briefed by their supervisors and provided with detailed written instructions for administering the questionnaire (Leonard, Tr. 87, 107-10; CX 1000, 1002).

103. The questionnaire for this study consisted of a notebook with 31 pages. Each page was a self-contained rating scale on a separate attribute, positive ratings at the top and negative ratings at the bottom. The rating of the products was to be made by the interviewees by inserting cards bearing the names of products into one of six pockets, corresponding to the intensity of their feeling about those products on each attribute (CX 346D, Z158-160).

104. The design of CX 346 was similar to that of other image studies commisssioned by DFS (Leonard, Tr. 86-88). And the "Assets and Liabilities" type of notebook-questionnaire used in this survey had been used by DFS since 1953 or 1954 for major clients such as General Mills and Falstaff Brewing Company (Miller, Tr. 214). This study design is comparable in quality to others for measuring images of products (Leonard, Tr. 94).

105. Validation of interviews at Crossley Surveys was a two-step procedure, conducted both by interview supervisors and then by Crossley's headquarters (Leonard, Tr. 110, 115, 138-39; CX 1001). This process provided a total of 15% of total interviews validated. As a third check on the interview-

ers' work, DFS itself validated an additional 10% of the interviews (Miller, Tr. 229-30).

106. Coding of the results of the survey was performed by Crossley's editing and coding department. A trained, experienced editor was normally responsible for that task. Given the absence of open-ended questions on the questionnaire necessitating interviewers' recording verbatim responses, coding for this project was a ministerial task. After the coding and editing tasks were accomplished by Crossley, the results were delivered to DFS, which analyzed them and prepared the report (Leonard, Tr. 115-16; Miller, Tr. 235).

107. The 1967 study was not conducted in anticipation of litigation. Sterling Drug, Inc. was DFS' client and requested the study in the regular course of business. Sterling was satisfied with the quality of the work and its presentation (Miller, Tr. 209-10, 235-36). Crossley Surveys itself had no direct contact with Sterling Drug, Inc. nor any interest in any particular outcome of the study (Leonard, Tr. 87).

2. *CX 310: The 1969 Excedrin Study*

108. The "1969 Excedrin Study" (CX 310) was designed by Young & Rubicam, Inc. for and in consultation with Bristol-Myers Company (Rosenbluth, Tr. 2865-66). It was a follow-up of an earlier survey conducted in 1966 and was intended to serve as a study of the penetration of Excedrin's advertising, of Excedrin's image among consumers, of the public's use of different brands of analgesics, and of consumer's "wants and needs" in analgesics (CX 310J-K).

109. Leon Rosenbluth testified for complaint counsel regarding the design of the survey. At the time CX 310 was conceived, he was the manager of survey research for Young & Rubicam, Inc. (Rosenbluth, Tr. 2856). Mr. Rosenbluth holds a Bachelor's degree in statistics from City College of New York and a Master's degree from New York University in sociology. He has had considerable experience in the design and analysis of market and advertising research (Rosenbluth, Tr. 2856-60). Young & Rubicam, Inc. is a major advertising agency with a research department that has performed adver-

tising research for numerous major corporate clients, such as Union Carbide, Remington and Proctor & Gamble (Rosenbluth, Tr. 2860). It is the advertising agency for Bristol-Myers for Excedrin.

110. William Nudorf testified for complaint counsel regarding the execution of CX 310. At the time the study was executed, Mr. Nudorf was field director of Grudin Appel, a full-service market research organization. His responsibilities included coordinating the fieldwork/interviewing tasks with the sampling and coding tasks associated with the study to insure that quality was maintained throughout. Mr. Nudorf and his subordinates did not know for whom the study was being performed (Nudorf, Tr. 2901-05). Mr. Nudorf holds a degree in journalism from the Pennsylvania State University, with a major in advertising. He had 14 years' experience in market and advertising research at the time the study was executed (Nudorf, Tr. 2898-2900). Grudin Appel was chosen by Bristol-Myers to execute the study. It had an excellent reputation among its clients and made consistent efforts to attract the best people in the market research field. Its clients included major advertising agencies, such as Young & Rubicam and BBD&O, and major consumer goods manufacturers, including General Foods, Gwaltney and ITT-Continental Baking (Nudorf, Tr. 2901-02; Rosenbluth, Tr. 2865, 2868).

111. Stanley Randall testified regarding the analysis of the survey results. At the time he analyzed those results for Young & Rubicam, he had been a research consultant with 15 years' experience in marketing and opinion research. His consultancy clients had included other major advertising agencies, such as J. Walter Thompson and McCann-Erickson, and his responsibilities involved all aspects of research from initial client contact to study design, questionnaire design, analysis, report preparation and presentation. Mr. Randall was hired by Leon Rosenbluth to analyze the results of the 1969 Excedrin Study on the basis both of excellent recommendations and of a review of initial drafts that he had worked on (Randall, Tr. 2978-80; Rosenbluth, Tr. 2871-73).

112. At the direction of Bristol-Myers, the sample for this survey was limited to Nielsen "A" and "B" counties (urbanized counties) across the United States (Rosenbluth, Tr. 2866). Grudin Appel was well-equipped to design and implement a probability sample of these urban areas. It had developed a master sampling plan based upon standard metropolitan statistical areas (SMSA's) and their contiguous counties (CX 1056). These areas accounted for over two-thirds of the national population. Interviews were apportioned to each U.S. geographic region based on that region's share of the total SMSA population. A sampling frame was constructed for each region, and within each region's sampling frame, sampling points were distributed over the population by using randomized procedures (Nudorf, Tr. 2932-45; CX 1056; CX 1057A-L).

113. Grudin Appel performed survey research using sampling procedures of this type on a frequent basis. This study therefore presented no unusual tasks to be performed (Nudorf, Tr. 2904-06).

114. Interviewers were given extensive instructions to implement the sampling plan. These instructions were sufficiently detailed to prevent the interviewers from exercising discretion in selecting respondents (CX 1057M-Q; Nudorf, Tr. 2942-44). This sampling procedure was typical of that used in other advertising penetration and image studies, and it produced a result that was projectable to all "A" and "B" counties in the United States (Nudorf, Tr. 2944-45).

115. The study was conducted according to Grudin Appel's regular standards of professional quality in all respects. The questionnaire was pretested and extensive instructions regarding its administration were given to interviewers. The instructions given to interviewers had been tested and proven in the past. By 1969, they were so standardized that Mr. Nudorf did not have to rewrite them for each survey. Rather, he would review them for their suitability for particular surveys (Nudorf, Tr. 2909- 30).

116. The interviewers used in this project worked for supervisors whom Mr. Nudorf had selected as the best he knew of in each metropolitan area; he had developed that level of familiarity and expertise in selecting supervisors over a 10-year period while he was employed by the research department of a major ad agency, traveling throughout the country doing advertising research (Nudorf, Tr. 2946). Interviewers were thoroughly trained to administer the questionnaire by their supervisors, who validated a portion of interviews after they were completed. Between 15 and 20 percent of all completed interviews were validated by Grudin Appel, and if any discrepancy arose in any portion of an interviewer's work, all of that interviewer's work would be validated. This validation was performed by Grudin Appel's in-house staff (Nudorf, Tr. 2948-50). The coding of the completed questionnaires was performed by Grudin Appel's large and experienced coding department. Tabulations of the coded questionnaires were performed by Donovan Data, a company with a good reputation for processing data (Nudorf, Tr. 2951-52).

117. Stanley Randall prepared the final report of CX 310.Before analyzing the data, he checked the coding of the questionnaires. He also checked the final tables prepared under his direction against the original tabulations before beginning any analysis for the final report. The final report of CX 310 was accepted by Young & Rubicam (Randall, Tr. 2985-92).

3. *CX 347/348: Study of Vanquish's Market Opportunities (1970)*

118. The 1970 "Study of Vanquish's Market Opportunities" was designed by Benton and Bowles, Inc., an advertising agency, for Sterling Drug, Inc., as part of the development of an advertising campaign for Vanquish. CX 347 was designed to measure consumers' attitudes toward analgesics in general, their opinion of some leading analgesic brands, including Vanquish, and to determine what sort of consumer Vanquish was most likely to attract (CX 347E).

119. Joseph Pernica, the Associate Research Director and Vice-President of Benton and Bowles, Inc. at the time had full responsibility for developing the design, methodology, and questionnaire for the survey, and for overseeing its execution (Pernica, Tr. 1893). He testified for complaint counsel concerning those areas. Mr. Pernica is an experienced market researcher who had devoted 10 years to the field by 1972. His experience includes six years as manager of market research for J. Walter Thompson, another major advertising agency. Mr. Pernica's academic background includes a Bachelor's degree in Business Administration from the University of Prague and a Master of Economics degree from Sydney University in Australia (Pernica, Tr. 1887-89).

120. Lieberman Research Corporation of New York was responsible for executing CX 347. Arnold Fishman, the Vice-President of Lieberman Research, testified for complaint counsel concerning the procedures used for conducting the study, including sampling procedures, interviewing, and coding and tabulating. Lieberman Research is a large marketing research company which also performs some public opinion research. Three-quarters to ninety percent of its work, however, is consumer research like the Vanquish study. Lieberman Research's consumer research clients include General Foods, Bristol-Myers, Sterling, and most of the major advertising agencies (Fishman, Tr. 1284). Lieberman had a high reputation for quality work with advertising agencies (Pernica, Tr. 1889). Arnold Fishman started as a Research Assistant and became a Vice-President of Lieberman Research after five years' experience with the organization. He holds a Bachelor's degree in Psychology from Brooklyn College and has completed all the requirements for a Master's Degree from City University of New York except his thesis (Fishman, Tr. 1281-82).

121. The sampling procedure for the 1970 Vanquish Study was developed by Lieberman Research according to specifications set by Joseph Pernica of Benton and Bowles. These specifications included the sample size, the number and type

of markets in which the survey would be conducted, and the desired 50/50 sex distribution of the respondents. Benton and Bowles instructed Lieberman to investigate the Mid-Atlantic and Pacific regions and also wanted to concentrate some interviews in three known high-share Vanquish markets, Atlanta, New Orleans and Oklahoma City. Lieberman Research was given a list of cities in the Mid-Atlantic and Pacific regions and chose the cities in which it had the best interviewers (Fishman, Tr. 1292-93; Pernica, Tr. 1918-19).

122. Within each market chosen, the sample was randomly selected from addresses listed in telephone directories. A random number was picked as the page on which to enter each phone book, and to get to successive pages, a skip interval equal to the number of remaining pages divided by the number of desired interviewing clusters was determined. In order to minimize the sampling error due to use of telephone listings, interviewers were instructed to interview a resident of the house adjacent to the one picked from the phone book (Fishman, Tr. 1299-1301). This procedure left no discretion to the interviewer in selecting respondents.

123. This sampling procedure was standard at Lieberman Research, and the sampling instructions given to interviewers were the company's standard written instructions (Fishman, Tr. 1339-40; 1300). It was not designed to produce a national probability sample. However, Lieberman considered the degree of deviation from strict adherence to all probability standards in this sampling pattern to be small and typically recommended that marketing decisions could be made based upon the data generated (Fishman, Tr. 1367-68).

124. The Vanquish Study was based on personal interviews. The questionnaire was carefully reviewed and revised by Arnold Fishman at Lieberman Research in order to eliminate ambiguities and to ensure correct question order. After it was put into final form, it was pretested in the field to ensure that it could be easily administered. The pretesting indicated that there were no significant problems with the interview (Fishman, Tr. 1295-97). Lieberman Research chose its inter-

viewers and supervisors carefully, using only supervisors who were known to have done timely work of high quality in the past, and encouraging the supervisors to use only their best interviewers. The supervisors were responsible for training interviewers, for passing on Lieberman Research's standard written instructions, for acting as intermediaries between them and the central office, and for validation of the interviewer's work. Lieberman did not rely solely upon the supervisor's validation, but validated an additional fifteen percent (15%) of all questionnaires in the central office. If validation of an interview uncovered a problem, all the work of that interviewer would be validated. In addition to these two validations, a third validation check was run by an outside service to ensure objectivity (Fishman, Tr. 1317-18).

125. Coding, keypunching and tabulations were performed by Lieberman Research according to its normal procedures for studies of this type. The codes for open-ended answers were developed by Lieberman Research's coding staff under Arnold Fishman's supervision. Joseph Pernica, of Benton and Bowles, approved the final codes (Pernica, Tr. 1929). A portion of every coder's work was checked by the coding staff supervisors to verify that coders were correctly interpreting verbatim responses (Fishman, Tr. 1319-21). Keypunching and tabulations were performed by Data Probe, a research computer company selected by Lieberman Research with the approval of Benton and Bowles, Inc. All of the coded questionnaires were "machine-cleaned" (checked for the logic of responses) and all the keypunching was verified by machine at Data Probe. Data Probe produced the tabulations of the results, CX 348, according to specifications set by Benton and Bowles, and Lieberman Research checked the tables for conformity with those specifications. Mr. Pernica received the tabulations from Lieberman Research and used them as the basis for his analysis presented in CX 347 (Fishman, Tr. 1321-25; Pernica, Tr. 1929-30).

4. *CX 326: 1971 Advertising Penetration Study*

126. CX 326, a telephone survey, was designed and analyzed by Ted Bates & Company, Inc., and was conducted by Valley Forge Information Services (hereinafter "Valley Forge"), for Bristol-Myers Corporation (CX 1019-20). Its purpose was to measure the advertising penetration of Bufferin and other OTC analgesics (CX 326C, E-K; CX 1009). The questionnaire design is typical of earlier Bates penetration studies, many of which were also performed for Bristol-Myers Corporation. Two other such studies were identified and cited as comparable, earlier penetration studies in the final report (CX 326D). Employees of both Ted Bates and Valley Forge testified that the questionnaire was typical of those used in assessing advertising penetration (Weitz, Tr. 731; Fratto, Tr. 810).

127. Ted Bates and Company, Inc. is the advertising agency for the Bristol-Myers Company for Bufferin. Ms. Anne Jack (formerly Anne Weitz),[3] a Vice President of Bates, testified for complaint counsel regarding the design and analysis of CX 326. Ted Bates' research department performs a wide range of research on all types of products for its clients (Weitz, Tr. 809). Ms. Jack has a Bachelor's degree from Holland College and a Master's degree from Duke University, both in psychology. She had worked for Ted Bates on research positions since 1960, and advanced within the agency from Project Director (in 1964) to Vice-President (in 1973). Her responsibility had included designing questionnaires since 1960 (Weitz, Tr. 807-10).

128. Valley Forge Information Services, a wholly owned division of Burlington Industries, is a market research firm with extensive experience in telephone surveys. Although it was originally formed in 1966 to work only for Burlington, it expanded to offer its services to other research companies, advertising agencies, and manufacturers, primarily involving

3 When Ms. Jack testified with respect to CX 326, during the Joint Hearings of 1977, her name was Anne Weitz (Jack, Tr. 6095). Accordingly, all citations which refer to her 1977 testimony appear here as "(Weitz, Tr.)"

telephone surveys (Fratto, Tr. 718-19). Kenneth Fratto was the President of Valley Forge from its inception until February 1977. He has a Bachelor's degree from Colgate University in Economics, and a Master's degree in Marketing from the Columbia Graduate School of Business. He worked in marketing research for Alfred Pollitz Research and Ogelsby, Benson Advertising Agency from 1957 to 1966, and rose to the position of senior vice-president in Alfred Pollitz Research in 1966. He has conducted over 300 studies in media research, product testing, advertising research, and market penetration (Fratto, Tr. 716-17).

129. The sample for the 1971 Ted Bates Advertising Penetration Survey was designed to be a national probability sample based upon telephone listings (CX 326Z004). Both Ted Bates and Valley Forge had done national probability samples before. Valley Forge had developed the capability for doing such samples during 1969-1970 and had done about one per month since then (Weitz, Tr. 819-20, 836).

130. Valley Forge designed the sampling plan for this survey very carefully. The first step was the construction of a "master probability sample." This was obtained by dividing up the entire country, according to published photostats from the Census Bureau, first into a census region, and then into four city-size classifications within the census regions. The "sampling points" within the four city-size classifications are randomly selected from within the counties listed in each classification. While one could obtain any number of sampling points, the one hundred points used in this survey were found more than adequate by Kenneth Fratto (Fratto, Tr. 737-38).

131. The telephone numbers of individual survey respondents were selected randomly from within these sampling points. Telephone directories were obtained from telephone companies for each county in the master sampling plan, a standing order being placed with each company to ensure that the directories were current. If, for example, 1,000 completed interviews were required, 2,500 numbers would be selected, 25 from each of the 100 sampling points in the master sample.

A randomized "skip pattern" within each phone book, starting from a random starting point, would also be established (Fratto, Tr. 738-40).

132. All interviewers were instructed orally about the correct way to select a particular column on a page and a particular number down in that column. In other words, the smallest detail was attended to as carefully as the drawing of the original master sample (Fratto, Tr. 739-41). In order to minimize a nonresponse bias, each number at which there was no response received two call-backs (Fratto, Tr. 744).

133. The questionnaire was easily administered, because it required no skips and very simple probes (CX 1009). Nevertheless, all interviewers received both written and oral instructions in conducting the interviews (CX 1021; Fratto, Tr. 740). In addition, training of the interviewers involved actual testing of their ability by supervisors who had at least one year's experience in interviewing and who were experienced in dealing with people (Fratto, Tr. 724). This degree of care in conducting interviews was a standard procedure at Valley Forge (Fratto, Tr. 720).

134. The interviewers' WATS lines were connected to a monitoring facility so that each interview could be listened to as it was conducted without the interviewers being aware of the monitoring process (Fratto, Tr. 742). In addition, all completed questionnaires were checked by Valley Forge's supervisors for thoroughness and accuracy. Finally, there would be a third check by a group of editors who would review the questionnaires before they were sent to the client (Fratto, Tr. 745).

135. Coding, keypunching and tabulation were performed by Ted Bates after it received the completed questionnaires (Fratto, Tr. 745). Because the questionnaires contained open-ended verbatim responses, Ted Bates employees expended a large amount of time and effort in developing appropriate codes for the verbatims despite the fact that the basic framework for coding had been developed during earlier Bates market penetration studies (Weitz, Tr. 823-24; CX 1016).

136. The mechanics of coding and tabulating were per-

formed by hand by Ms. Jack herself and a trainee under her close supervision (Weitz, Tr. 826).

5. *CX 345: The 1973 Headache Remedy/ Pain Reliever Usage And Advertising Penetration Study*

137. CX 345, a telephone survey, was designed to determine current advertising penetration and usage levels of selected analgesics (CX 345C). The study was designed, executed and analyzed by Sobel-Chaikin Research Associates at the request of and in cooperation with American Home Products Corporation (Sobel, Tr. 461-64). Sobel-Chaikin Research Associates is the research division of Market Probe International (hereinafter, "M.P.I."), an organization formed in approximately 1964 to perform market research, computer analysis and data processing for manufacturers and advertising agencies. Its major clients include Pan American Airlines, IBM, Citibank, and Doyle Dane Bernbach (Sobel, Tr. 451-53). Charles Sobel testified for complaint counsel regarding both the design and the execution of CX 345 for which he had ultimate responsibility. Mr. Sobel is Senior Vice-President and Director of the research group at M.P.I., and the founder of Sobel-Chaikin Research Associates. At the time of the survey, he had approximately 23 years' experience in market survey research similar to CX 345. Indeed,almost every consumer survey that Mr. Sobel had been involved in had some questions that related to advertising penetration (Sobel, Tr. 447, 451-52, 455, 457-66).

138. The study design called for a telephone sample to be randomly selected from telephone directories in 10 major urban markets (CX 345C; CX 1007; Sobel, Tr. 467-68). Interviewers in each market were assigned a random starting page in the telephone book for that market and were instructed to skip a random interval number in order to obtain each succeeding page (CX 1007). They were instructed to start at the top of the second column of each page and proceed down the column until they had completed a series of five interviews. These

instructions left no discretion to the interviewer in the selection of respondents (Sobel, Tr. 467-68).

139. The questionnaire for this survey was short, and it was easy to administer because it contained few skip patterns for interviewers to follow (CX 345 Z101-104). The questions were unambiguous and were directed both to advertising recall and usage of analgesics. The questionnaire was developed in consultation with American Home, and was typical of those used previously by Sobel-Chaikin for advertising penetration studies (Sobel, Tr. 461-62; 484).

140. The survey was conducted according to standardized procedures followed by Sobel-Chaikin Associates in all their research work. All interviewers received extensive instructions regarding the administration of the questionnaire and were personally trained by supervisors who were known to the principals of the firm or to one of their field supervisors, on the basis of prior favorable experience (Sobel, Tr. 471-72). Completed interviews were validated in a two-step procedure. Supervisors were instructed to validate work received from all their interviewers. In addition, 15% of the completed interviews submitted by supervisors were validated by an outside validation service hired by Sobel-Chaikin (Sobel, Tr. 477-81).

141. M.P.I.'s in-house coding department coded the responses on the completed questionnaires. The task involved building codes for verbatim responses to open-ended questions on the questionnaire asking about advertising recall. The final codes were prepared by Mr. Sobel and were approved by American Home. Checks on the quality of coding were supplied by M.P.I.'s coding supervisor and by having individual coders redo each other's work for comparison purposes (Sobel, Tr. 483-85; CX 1005-06).

142. M.P.I.'s own data processing group keypunched the completed questionnaires. The keypunching was performed by experienced operators and was checked both by verification and by automatic controls placed into the computer programming that produced the tabulation runs. The tabulation plan was developed in accordance with specifications approved by

American Home Products. The report of CX 345 was prepared by Mr. Sobel and was submitted to American Home (Sobel, Tr. 484-87).

6. *CX 349: "The Leavitt Study" (1975-1976)*

143. Dr. Clark Leavitt, an expert witness in the design and analysis of research which measures consumers' images and beliefs about products (Leavitt, Tr. 6160-72; CX 701), testified concerning a consumer telephone survey he designed for the Federal Trade Commission.

144. Dr. Leavitt holds a Ph.D. degree in Social Psychology from the University of California. He has taught at two colleges and now teaches at the Ohio State University, concentrating in various subdisciplines of psychology including social psychology, consumer behavior and research methodology (Leavitt, Tr. 6160-62). He supervises graduate and post-graduate student research and conducts research for publication in professional journals (CX 701). He also currently designs and conducts applied research as a consultant for clients, including advertising agencies (Leavitt, Tr. 6166-69).

145. Dr. Leavitt has had extensive experience in the design and implementation of consumer ressarch related to effects of advertising and to consumer attitudes and images about products. He has worked in marketing and consumer research for two advertising agencies, E.H. Weiss & Co. (1955-1957) and Leo Burnett Company (1957-1972). At Weiss, Dr. Leavitt conducted exploratory consumer research on basic consumer beliefs and motives, and the relationships between advertising, public awareness and sales. At Leo Burnett, he supervised all marketing research for a group of clients, and became creative research supervisor and thereafter Director of the Communications Laboratory. He was responsible for the design of marketing research for all of Burnett's clients, including Proctor & Gamble, Pilsbury, Carter-Wallace, All-State Insurance, Motorola, Pfizer, and manufacturers of drug products. Research for many of these clients concerned consumers' purchases and opinions about products and their awareness of ad-

vertising, and many of his projects have involved the development of rating scales to measure consumer perceptions or predispositions. He has supervised or conducted thousands of studies which test consumers' beliefs and attitudes (Leavitt, Tr. 6162-65).

146. Dr. Leavitt's own research has involved the measurement of the relationship between the advertising and the stability of people's opinions or attitudes; other research involves distributions of advertising schedules, patterns of forgetting with respect to advertising, and source credibility. At least 50% of the articles he has published in professional journals have involved research measuring attitudes, beliefs or images. Dr. Leavitt is an active member of the American Marketing Association, the Association for Consumer Research, the American Psychological Association and the American Association for Public Opinion Research. He is a former President of the Division of Consumer Psychology of the American Psychological Association and has served on the editorial boards of various professional publications (Leavitt, Tr. 6166-70; CX 701).

147. Dr. Leavitt is well qualified as an expert in the design and analysis of consumer research which measures consumer images, beliefs and attitudes about products (F. 144-46, *supra*).

The Design of the Study

148. Unlike the other image studies in evidence, the questionnaire and methodology of CX 349 were designed by Dr. Leavitt to measure respondents' *comparative* beliefs about the effectiveness, speed, strength and gentleness of Bufferin, Excedrin, Anacin and aspirin. The products and the four performance attributes that he surveyed were specified by the FTC staff before he began to design the study (Leavitt, Tr. 6173-77). The control of response bias was one of Dr. Leavitt's primary considerations in the design of the questionnaire (Leavitt, Tr. 6178-81).

149. The effect of Question 1 of Dr. Leavitt's questionnaire was to inform respondents that they would be asked about four separate products in the survey: Anacin, Bufferin, Excedrin and aspirin (CX 349W). The word "aspirin" was chosen by Dr. Leavitt as a product to rate along with Bufferin, Excedrin and Anacin because of his understanding of the nature of this case as explained by complaint counsel, and because of his belief that for the purposes of the study, the word "aspirin" was the most sensible one (Leavitt, Tr. 6179-81, 6187, 6191).

150. Questions two (2) through five (5) of the Leavitt questionnaire set forth the basic rating scale constructed by Dr. Leavitt to measure consumers' beliefs about these products on the four attributes of interest. The scale consisted of four verbal points: "extremely," "very," "fairly" and "not." Consumers were asked to rate the effectiveness, speed, strength and gentleness of each of the four products on this scale (CX 349W; Leavitt, Tr. 6182-85). His method permitted a conclusion about comparative image held by individual consumers about the four products without asking them a direct but leading question about their comparative image with regard to a particular product attribute.

151. A comparative question such as "Do you believe that Bufferin is a more effective pain reliever than aspirin," could have produced biased results (Leavitt, Tr. 6179). For one thing, such a direct, comparative question suggests that Bufferin and aspirin do perform differently (Leavitt, Tr. 6179-80). Moreover, there are general tendencies, or "sets," among many consumers to answer "yes" throughout or "no" throughout to all interview questions that are put to them in that form (Leavitt, Tr. 6180). This positive or negative set may manifest itself in uniform answers to "yes/no" questions regardless of what the substance of the question is. Asking absolute or neutral questions of respondents avoids this bias (Leavitt, Tr. 6180-81).

152. The four-point rating scale used in the Leavitt questionnaire provides an acceptable measure of the intensity of a consumer's belief about a product on a particular attribute. The

four points in the scale have an ordinal relationship to each other in the sense that "extremely" ratings are appreciably more intense than "fairly" ratings, which are in turn more intense than "not" ratings (Leavitt, Tr. 6182-83). Based on his experience, Dr. Leavitt believed that the four point scale should provide for more positive responses ("extremely," "very" and "fairly") about a product than negative ones ("not") because people tend ordinarily to rate products more positively than negatively. Accordingly, more steps on the positive side of the scale are necessary to compensate for this predisposition (Leavitt, Tr. 6183-84).

153. A neutral response was not included in the scale in order to increase the sensitivity of responses. It is known that some portion of the population tries to avoid either a positive or negative response to particular questions asked in a survey. Failure to provide for a middle-of-the-road response overcomes that tendency and encourages a true response (Leavitt, Tr. 6184).

154. Dr. Leavitt had considerable experience with rating scales using the four adjectives used here (F. 153, *supra*; Leavitt, Tr. 6182-83). Based upon his review of the literature and upon his extensive experience, he concluded that the steps on a rating scale ought to be anchored by verbal descriptions rather than by simple numbers like a thermometer (Leavitt, Tr. 6182-83). He had found that a verbally anchored scale produced more reliable, more stable kinds of data than other scales he had tried which relied upon numbers or other techniques to anchor its points (Leavitt, Tr. 6183).

155. Because the ratings of products in a series may be effected by the order in which the products are presented (order or position effects), the study design included a control on that bias by rotating the order in which products were presented to respondents for rating. One quarter of the sample started out with each different product out of the four and ended with each different product (Leavitt, Tr. 6180, 6188-89; Crespi, Tr. 2274, 2276; CX 349W, CX 352B).

156. On the other hand, the order of presenting product attributes (as opposed to products) was not rotated because Dr.

Leavitt believed it was necessary to start all interviews with a specific performance attribute rather than a general one. "Effectiveness" is a general attribute in the sense that it evokes consumers' overall assessment of an analgesic product (Leavitt, Tr. 6189). Asking for a general rating first may produce another type of response bias, *i.e.*, creating an early commitment in a respondent to an overall favorable or unfavorable evaluation of a product that would affect his subsequent ratings of other attributes (Leavitt, Tr. 6189). In order to avoid this bias, the attributes were presented in the order of increasing generality, from "gentleness" to "effectiveness" (Leavitt, Tr. 6189; CX 349W). And, because the order in which the products were presented was rotated, any consequence of the fixed order in presenting attributes for rating would have been spread equally across all products.

The Execution of the Study

157. Dr. Leavitt determined the basic specifications for the field work of CX 349, including the number of interviews and the sample procedures. Between 700 and 800 interviews were decided upon to assure that there would be enough responses to conduct meaningful analyses which could be generalized beyond the sample itself (Leavitt, Tr. 6186; Crespi, Tr. 2280). In Dr. Leavitt's opinion, telephone interview was the best way to obtain the information needed in the study (Leavitt, Tr. 6186).

158. Dr. Leavitt approved the selection of the Gallup Organization to conduct the field work for this study because he believed it was an organization that had considerable experience in drawing representative samples of the type he was considering. He was also familiar with the excellent reputation of Dr. Irving Crespi, his contact at Gallup Organization (Leavitt, Tr. 6175-76). Dr. Crespi testified regarding the sample design, its implementation and about the field interviewing procedures used by the Gallup Organization in the study. At the time of the study, Dr. Crespi was Executive Vice President of Gallup (Crespi, Tr. 2268).

159. The Gallup Organization specializes in marketing, consumer and public opinion survey research for clients which include many of the major consumer goods manufacturers and marketers in the United States (Crespi, Tr. 2262-63). It also conducts the "Gallup Poll." Dr. Crespi received a Ph.D. degree in Sociology from the New School for Social Research. He had been employed at Gallup for 20 years and was involved in all aspects of the organization's survey research functions, including the development of questionnaires, the proper implementation of survey design, the reporting of results and maintaining client contact. He has been personally involved in marketing research for numerous major corporations. Dr. Crespi had risen to the position of Executive Vice President at the time he left Gallup in April 1976, and he maintained direct supervisory responsibility for survey research projects until he left. Dr. Crespi has been a member of the Board of Directors of the American Marketing Association; he is past President of the American Marketing Association; he is past President of the American Association for Public Opinion Research; and, at the time of his testimony, was President of the World Association for Public Opinion Research. He has published several articles dealing with consumer research in professional journals in the marketing field (Crespi, Tr. 2262-65; CX 702). Dr. Crespi is well qualified as an expert in the execution of consumer research.

160. Dr. Crespi obtained specifications from Dr. Leavitt and complaint counsel regarding the number of interviews to be conducted, the fact that the survey was to be conducted by telephone, the fact that the people under 18 were not to be interviewed, the fact that people who were not aware of at least one of the four products surveyed were not to be interviewed, and the fact that the sample of between 700 and 800 was to be projectable (Crespi, Tr. 2268, 2277-79; Leavitt, Tr. 6191-92).

161. After receiving Dr. Leavitt's questionnaire, Gallup reviewed it and pretested it to see that it conformed to good professional practice. The pretest led to Gallup's recommending some modifications. The pretesting disclosed that some respondents were unwilling to rate products because they had

not personally used them, and the introduction to Question 2 (the beginning of the rating scale) was changed to emphasize that the interviewer was seeking their product images regardless of whether they used the products (Crespi, Tr. 2269-70; CX 349W). Other minor modifications were made in the introduction to the interview, in Questions 7 and 8, and in formulating the questions designed to obtain the demographic characteristics of the respondents. Based upon Dr. Crespi's experience, the modified questionnaire was a standard questionnaire using techniques representing the norm in brand image research (Crespi, Tr. 2277).

162. The population of telephone numbers that was sampled by Gallup was generated by adding a random digit to the telephone number of respondents who had been previously interviewed in their homes for the Gallup Poll (Crespi, Tr. 2282-84). The sampling design used for the Gallup Poll is carefully designed to remove any personal judgment or discretion of the interviewer as to whom to interview. The Poll is based upon a sampling of people at three hundred (300) separate, randomly selected points throughout the country. Sampling points are either city blocks (in urban or metropolitan areas) or minor civil subdivisions (in rural areas). Each interviewer for the Poll is given a randomly selected starting assignment at a particular sampling point, and is given instructions on how to proceed from residence to residence. This procedure produces a sample of households whose results are reasonably projectable to all households in the nation at large (Crespi, Tr. 2285-88). To develop the reservoir of telephone numbers actually sampled in the Leavitt Study, a random digit (the number "5") was added and subtracted to the last digit of the telephone numbers of these sampled households. This procedure produced a sample of residential telephone households which reasonably represents the national population of telephone households (Crespi, Tr. 2288; Leavitt, Tr. 6191-93).

163. The population sampled in the Leavitt Study was limited to people over 18 years of age who were aware of at least one of the four named products. Accordingly, the tele-

phone sample used is representative of the people over 18 who live in households with telephones and who heard of at least one of the four products, aspirin, Anacin, Bufferin and Excedrin (Leavitt, Tr. 6192-93).

164. Interviewers who conducted the telephone interviews were given the actual telephone numbers obtained in the Gallup Poll and written instructions on how to generate the telephone numbers to be called in this study. They were required to record each of the telephone numbers they generated and each of the numbers of the households where they completed an interview. If a generated number was busy, or there was no answer, or a respondent of proper age was not at home, the interviewers were instructed to call back in another attempt to complete the interview (CX 352A-C). The rate of interview refusals and break-offs in this survey conformed with Gallup's experience in other telephone surveys. The overall interview completion rate of 50% is rather low, but Dr. Crespi testified that it conformed to Gallup's experience in studies of this type where two attempts are made to complete an interview (Crespi, Tr. 2295-96; CX 1053).

165. The telephone interviewers used in this Study worked for Gallup on a regular basis and their work was subject to systematic quality checks by Gallup directly. The interviewers were supervised by an interviewing department at Gallup under an experienced supervisor with specific responsibility for the telephone interviewing staff (Crespi, Tr. 2288-90). The interviewers were unaware of both the purpose and the sponsors of the study (Leavitt, Tr. 6190). The interviewers were under strict instructions not to deviate from the wording of the questionnaire in any way. If a respondent did not understand a question the interviewer was instructed to read it again but not to reword it (Crespi, Tr. 2292). With respect to Questions 1 through 6, all the interviewer had to do was check the appropriate response box precoded on the questionnaire. With respect to Question 7, an open-ended question, interviewers were instructed to write down the respondents' answers verbatim. Therefore, interviewers were given no discretion whatsoever in the conduct of the interview (Crespi, Tr. 2292-93). An

8% subsample of all interviewees was recontacted by Gallup, who verified that the interviews had taken place and on the proper topic. Gallup's interviewers' work had been regularly validated by this technique in their previous work experience with Gallup and had been shown time and again to be genuine (Crespi, Tr. 2293-94).

166. The responses recorded by interviewers were coded by Gallup's experienced coding department. The questionnaire was precoded to a significant degree, which reduced both the opportunities for interviewer discretion and the complexity of the coding task. Interpretative codes were used only for responses to Question 7, which dealt with respondents' uses of aspirin, Bufferin, Anacin and Excedrin for things other than pain relief (Crespi, Tr. 2292, 2297-98). Keypunching was done by Gallup internally. The keypunched cards were verified according to Gallup's standard procedures, and the data were checked for inconsistencies, or "edited." If any inconsistencies were found, they were either edited by the computer while tabulating the data, which is Gallup's standardized editing process, or the original questionnaires were checked. There were no editing problems with this study (Crespi, Tr. 2304). At the conclusion of its assignment Gallup delivered a "clean deck" of punched cards to Dr. Leavitt, together with supporting materials on interviewing procedures and the keypunching plan (Leavitt, Tr. 6196; CX 351, CX 352).

167. The Leavitt Study was designed and executed by highly qualified personnel, experts in their respective fields, according to well recognized standards in the industry and using procedures consistent with these individuals' prior extensive experience in the design and execution of survey research. The results of the survey are reliable and probative on the issues to which they are addressed.

7. CX 343, 344, 1058, 1059: The Attitude Study In Depth of Heavy Users of Analgesics and Follow-Up

168. CX 343 and its follow-up, CX 344, were performed in 1967 and 1970 by Oxtoby-Smith, Inc. for Whitehall Laboratories, a division of American Home Products Corporation. They were designed by Oxtoby-Smith to study the images of OTC analgesic products among consumers, under the supervision of Martin Weinberger, the Research Director, who testified for complaint counsel regarding the design, execution and analysis of CX 343 and 344. Mr. Weinberger has 15 years' experience in designing and executing consumer attitude studies at Oxtoby-Smith and was involved in approximately 1,000 such studies during his career with that organization. In addition to his practical experience at Oxtoby-Smith and another major research organization, Mr. Weinberger holds a Bachelor's degree and has done graduate work in public opinion research at Columbia University (Weinberger, Tr. 5205).

169. Oxtoby-Smith is one of the largest custom-design consumer research organizations in the U.S. It designs and executes research for a wide variety of clients and product categories. The organization focuses on decisions about consumer attitudes and behavior (Weinberger, Tr. 5206). CX 343 was conducted in 1967, at the request of American Home Products' research director; thereafter Oxtoby-Smith was called upon to do a follow-up study in 1970 (Weinberger, Tr. 5219).

170. CX 343 and 344 were conducted according to Oxtoby-Smith's standard procedures for surveys of this type. The interviewers conducting the survey were personally trained by their supervisors. The supervisors themselves had generally been used by Oxtoby-Smith in the past, or they were recruited for this study based upon their reputation with Oxtoby-Smith's field directors (Weinberger, Tr. 5225).

171. The questionnaires for the two studies were drafted by Mr. Weinberger and were approved by Whitehall's research director (Weinberger, Tr. 5219-20). The questionnaires were pretested according to Oxtoby-Smith's standard procedures (Weinberger, Tr. 5220-21).

172. The sample for the study was designed to concentrate on heavy users of analgesics. The term "heavy" was defined

as those consumers who took six or more pain relievers for headaches in the two-week period prior to interview. Equal quotas were set for each of the leading analgesic brands, and for users of nonleading brands, and for "light" (under six pills) users of analgesics. This quota sample design was employed, at least in part, to eliminate the possibility that unequal numbers of users of the brands studied might bias the results of the survey as a whole (Weinberger, Tr. 5223-24). Interviewers were instructed to proceed on a house-to-house basis until they filled their quotas of various users (Weinberger, Tr. 5226). These sampling procedures were developed in consultation and with the approval of Whitehall (Weinberger, Tr. 5228). The sample was taken in 21 cities (CX 343Z085; Weinberger, Tr. 5224).

173. The completed questionnaires were returned to the interviewers' supervisors who validated 15% of all interviews done in that city. Thereafter, the questionnaires were returned to Oxtoby-Smith and an additional 15% of interviews were validated. These were standard validation figures for Oxtoby-Smith (Weinberger, Tr. 5251-52). Coding was performed internally under the direction of coding supervisors in Oxtoby-Smith's coding department (Weinberger, Tr. 5253-54). Keypunching of those coded responses was also performed internally with standard procedures employed to check on its accuracy (Weinberger, Tr. 5254). The punched cards were thereafter sent to an outside tabulation house for computer processing (Weinberger, Tr. 5258). The end product of this process was the series of tabulations in evidence as CX 1058 and 1059. Mr. Weinberger then drafted reports which analyzed this data and presented them to his client (Weinberger, Tr. 5256).

B. Survey Research Measuring Consumers' Awareness of the Ingredients in Bufferin and Excedrin

1. *CX 333: Consumer Use of Headache Remedies and Knowledge of Their Ingredients*

174. The 1964 study, "Consumer Use of Headache Remedies and Knowledge of Their Ingredients" (CX 333), was de-

signed, conducted and analyzed by the Gallup Organization, Inc., for Bristol-Myers Company. It was designed to measure consumers' awareness of the ingredients of eight major analgesic products, and especially their knowledge as to whether Bufferin contained Di-Alminate as its advertising campaign stressed at the time. In addition, it measured the extent to which consumers knew that these products contained aspirin (CX 333A, C, D).

175. Dr. Irving Crespi, who was Executive Vice-President of The Gallup Organization, Inc., in 1964, testified regarding the design and execution of the survey. His credentials, and those of The Gallup Organization, Inc., in the field of market research are excellent (F. 159, supra).

176. The sampling plan was designed to produce a national probability sample of the adult civilian population 21 years old and over (CX 333C). This plan was used regularly by The Gallup Organization, and differed only in two minor details from that used subsequently in 1975 in CX 349 (F. 162, supra). First, the minimum age for respondents had been lowered from 21 to 18 by 1975, and second, the two original 150-point master samples used in 1964 had been merged by 1975 into one 300-point master sample (Crespi, Tr. 2326).

177. The questionnaire used in CX 333 was easy to administer. It was short and contained no skip patterns. The questions eliciting unaided answers were short and clear. The order of questions asked about the four major brands was rotated in order to control the order effects (CX 333C, D). The questionnaire was pretested according to Gallup's standard procedures. Two or three interviewers conducted three to six interviews each and then attended a debriefing session with Dr. Crespi to discuss the pretest (Crespi, Tr. 2324).

178. The interviews were conducted according to The Gallup Organization, Inc.'s standard procedures. First, every individual interviewer was tested in a trial assignment process before he or she could become a member of Gallup's regular interviewing staff; only members of this staff were assigned to work on the 1964 survey. Second, interviewers for this study

were provided with extensive written instructions in the Interviewer's Bulletin. Third, almost all supervision was conducted out of Gallup's central office, so that the supervisors reported directly to headquarters. Finally, a high percentage of completed interviews (20 to 30%) were validated by postcard (Crespi, Tr. 2327-29). Procedures for coding and keypunching were identical to those used in CX 349 in 1975 (Crespi, Tr. 2331; F. 166, *supra*). Tabulations of the responses were either done internally by Gallup on its counter sorter or by an outside computer company to Gallup's specifications (Crespi, Tr. 2331-32). The resulting tables, apart from accompanying analysis, are to be found on pages F, H, J, K, L, and O of CX 333.

2. *CX 314: Pain Reliever Telephone Study*

179. The 1972 "Pain Reliever Telephone Study" (CX 314) was designed by Bristol-Myers Company to measure consumer usage of analgesics in general, their opinions of major brands, and their awareness of news reports about analgesics, and was conducted by Edward Blank Research Company for Bristol-Myers Company (CX 314A). Of special importance to this case, the study also measured consumers' knowledge of the ingredients of five leading brands of OTC analgesics (CX 314Z019-Z021; Blank, Tr. 2666-67).

180. Edward Blank testified for complaint counsel as to the execution of the 1972 survey by the Edward Blank Research Company, of which he is founder and president. His experience in the field of market research includes the design and conduct of survey research for National Broadcasting Company concerning the effectiveness of their advertising, and the design of consumer studies for Benton and Bowles Advertising Agency. Immediately prior to forming his own company, he was manager of marketing information for ROYFAX, an office copier manufacturer. He holds an undergraduate degree in economics, and has taken graduate courses in marketing research from New York University's Graduate School of Business (Blank, Tr. 2658-63).

181. Edward Blank Research Company, formed in 1969, has performed research for several leading corporations and advertising agencies, including Gillette, Continental Can, and Doyle Dane Bernbach. Mr. Blank has been personally involved in all of the nearly two hundred studies it has conducted (Blank, Tr. 2662-63).

182. The sampling procedure used by Edward Blank Research Company for the 1972 survey was designed to be generalizable to all adults in telephone households within five major urban markets (New York, Atlanta, Chicago, Denver, and San Francisco). The sampling plan was a standard procedure with Edward Blank Research Company and met the requirements of Bristol-Myers Company (Blank, Tr. 2668-70). Within each of the five urban markets selected, a quota of 60 women and 40 men over 18 were to be interviewed. Respondents were selected randomly from the market's telephone book by interviewers who were given straightforward written sampling instructions. Each interviewer was assigned a randomly selected starting page, column, and line and was instructed to contact the person so identified. Then the interviewer was instructed to get to the next page of the book by skipping a number of pages equal to the total number of pages in the telephone book divided by one hundred. The interviewer was instructed to select the next respondent from the identical location on that page as on the previous one. These instructions left no discretion to the interviewers in selecting respondents (Blank, Tr. 2665-72).

183. Edward Blank himself took steps to insure that the interviews for CX 314 were conducted competently. First he worked on the questionnaire he received from Bristol-Myers so that it would be easy to administer and the questions would flow in a logical sequence. The resulting questionnaire is a simple one, consisting almost entirely of multiple choice questions. It required only that the interviewer check a box to record respondent's answer. In addition, there are interview administration instructions included on the questionnaire itself (Blank, Tr. 2663-67; CX 314Z019-21). The telephone interviewing was contracted out to independent interviewer super-

visors in the five markets sampled. Blank chose only those supervisors he knew to have competent interviewers on their staffs either from prior experience or recommendations. Fifteen percent (15%) of all completed questionnaires were validated by an independent WATS-line company (Blank, Tr. 2669-75).

184. Coding and tabulating were performed according to Edward Blank Research Company's standard procedures. The company's own coding department developed a coding system for verbatim responses after studying at least one hundred responses to each question. After the code was developed, and after its approval by Edward Blank, the mechanics of coding would be performed under the guidance of the department supervisor. Tabulation of the coded questionnaire was performed by DATATAB, a data processing company selected by Blank based upon prior satisfactory experience. The tabulations were performed acccording to specifications given to DATATAB by Edward Blank, who checked DATATAB's work for conformity to instructions and accuracy, and the tabulations were delivered to Bristol-Myers Company (Blank, Tr. 2677-81). The final report consists mainly of 24 tables which measure consumers' use of, awareness of advertising for, and knowledge of the ingredients of OTC analgesics (CX 314D, F-Z018).

C. Survey Research of Audience Reaction and Recall

1. *The ASI Audience Reaction Tests*

185. The 17[4] ASI Audience Reaction Tests in evidence were conducted by Audience Studies, Inc., (hereinafter "ASI") on television advertisements for Bufferin, Excedrin and Excedrin P.M. to measure their effectiveness. The tests are of standardized design, and seek to evaluate consumer reactions to advertisements in terms of persuasiveness, involvement and recall (CX 811A, B).

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4 CX 245, 246, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 261, 262, 263, and 264.

186. Gerald Lukeman, ASI's President, testified for complaint counsel concerning the design and general procedures of ASI testing. Mr. Lukeman has primary responsibility for sales and service; he also is involved in modification of the design of the testing when necessary. Mr. Lukeman has worked at ASI since 1953, having had three years' experience with a predecessor, the Schwerin Company. Prior to joining ASI, he earned a Bachelor's degree from Dartmouth College with a major in Psychology (Lukeman, Tr. 4303-04). ASI's field of expertise involves research in communications, especially advertising (Lukeman, Tr. 4305). It has measured the effectiveness of advertising in all of the commonly used media, and it tests audiences' reactions to approximately 1,500 commercials every year. Its clients vary greatly in size, but tend to be the nation's largest manufacturers and advertising agencies (Lukeman, Tr. 4305-06). ASI has conducted tests on commercials for OTC analgesics at a minimum frequency of 70 tests per year for at least 10 years (Lukeman, Tr. 4306-07). During the time the ASI studies in evidence were conducted, Mr. Lukeman supervised the Bristol-Myers account and was responsible for the proper execution of the tests, as well as the follow-up with the client regarding the nature of the resulting data (Lukeman, Tr. 4311).

187. Except for CX 264, all of the ASI studies were conducted in Los Angeles. CX 264 was a test performed in St. Louis on a "David Janssen" advertisement for Excedrin P.M. ASI tested the identical "David Janssen" ad in Los Angeles (CX 263). This substitution of cities was due to the fact that David Janssen ads for Excedrin were being televised on the West Coast, and ASI wanted to test the effectiveness of Janssen's ad for Excedrin P.M. in both exposed and unexposed geographic areas to see if differences existed (Lukeman, Tr. 4315). Like all of the studies, CX 264 was analyzed by ASI's Los Angeles staff (Lukeman, Tr. 4315).

188. The stipulated testimony of Roger Seltzer concerned the mechanics of conducting the Audience Reaction Tests (CX 811). Mr. Seltzer supervises ASI's Los Angeles office which is

responsible for ensuring the appropriate execution of the tests (Lukeman, Tr. 4313-14). Audience Reaction Tests were conducted according to a procedure which remained virtually unchanged from 1967 to 1973 (Seltzer, CX 811B). Except for CX 264, the tests were conducted in a theatre in Los Angeles, housing an audience of approximately 350 respondents. The audience for CX 264 was recruited from the St. Louis metropolitan area, where testing for that advertisement was conducted (Seltzer, CX 811C; F. 187, *supra*). The audience for each test was recruited, either in person or by telephone, to attend a preview of television programs, with no charge or obligation except that they would be asked for their opinions of the programs they saw (Seltzer, CX 811C). As the audience entered the theater they were given seats, and according to ASI's standard procedure, certain respondents were selected by ASI personnel to operate the dials of a recording machine at their seats designed to measure their reactions to the materials they viewed. A second subsample was sometimes selected to have their reactions to materials they viewed monitored by basal skin resistance recorders which were at their seats. A third subsample was selected to participate in a "focus group" discussion held at a point in the evening after the commercials had been viewed (Seltzer, CX 811C, D).

189. Each member of the audience was given a questionnaire folder and while seating was being completed, he or she was asked to answer questions about various demographic characteristics and use and preferences for different brands of products. Finally, each respondent was presented a list of products and asked which he/she would prefer to receive as a door prize (see, *e.g.*, CX 254Z024-027) (Seltzer, CX 811D).

190. After the respondents have filled out the preliminary questionnaires, they were shown a "control" cartoon (Seltzer, CX 811D-E; F. 191, *infra*). Next, they were shown a regular length television program. Those with dials reacted to the program by manipulating the dials, and at the conclusion of the television proqram all audience members were asked to fill out a questionnaire about the program. It is ASI's practice not to

include the results of this questioning in its reports (Seltzer, CX 8IIE). After the television program was shown, the audience was told that it would be seeing a series of five commercials (''commerical'' material), and a five section commercial questionnaire booklet was distributed (Seltzer, CX 8IIE). Then the first commercial was shown. Following the showing of this first commercial the audience filled out the first section of its five page questionnaire (see, *e.g.*, CX 254Z028-029). This procedure continued until the audience saw all five commercials and completed all five sections of the questionnaire (Seltzer, CX 8IIF). After the five commercials, the audience was shown a second television program segment and filled out a short questionnaire regarding it (Seltzer, CX 8IIF). Thereafter the audience, given the impression that the pre-selection questionnaire (F. 189, *supra*) was the incorrect one, selected from a new questionnaire the product they would like to win as a door prize (see, *e.g.*, CX 254Z030). This second, or ''post-selection,'' prize questionnaire was then collected (Seltzer, CX 8IIF). Thirty or forty minutes after viewing the commercials, the audience was given a ''recall questionnaire'' which asked them to write down all they recalled about the five commercials they saw earlier, including the products, brand names, and details of the ads (see, *e.g.*, CX 254Z031). After the ''recall questionnaire'' was collected, door prizes were awarded, and the evening was concluded (Seltzer, CX 8IIF, G).

191. Several controls used on the night of the presentation are designed to minimize any sampling error that may have arisen in the selection of respondents. First, of the 350 viewers in the audience who fill out questionnaires, usually only 250 will be used. This is because certain segments of the population tend to be overrepresented in the theater audience, and ASI requires that the sample it analyzes approximate a distribution which is comparable to samples previously recruited and tested by ASI (Seltzer, CX 8IIC). The second control involves use of a cartoon which has been used as a standard for most ASI sessions. The use of a ''control'' cartoon permits those in the segment of the audience using dials to learn to ma-

nipulate them; it also permits ASI employees to compare this audience's dial reactions to the same material (the same "control" cartoon) reacted to by many other audiences. If the audience's reactions to the "control" cartoon do not satisfy ASI that this audience is reacting in reasonable accord with norms based on past audiences' reactions, the data generated through the subsequent questionnaire regarding "program" material is discarded, and that program material retested at a later date (Seltzer, CX 811D-E). Finally, as with the "control" cartoon, the first commercial shown is always a "control," *i.e.*, a commercial tested many times previously for which audience reaction is known. Like the "control" cartoon, ASI monitors the audience's reaction to the first "control" commercial to determine if it is reacting within normal limits established through ASI's prior experience with reactions to this same commercial. If the audience's reactions to the "control" commercial do not satisfy ASI that this audience is reacting in reasonable accord with norms based on past audiences' reactions, the data generated through subsequent questionnaires regarding the "commercial" material is discarded and that commercial material retested at a later date (Seltzer, CX 811E-F).

192. The procedure described above (F. 188-91, *supra*) applied to everyone in the audience except the 10 to 12 people chosen earlier for the group discussions; they were taken from the theater after viewing the commercials and, in a session led by a trained ASI moderator, they discussed, among other things, the commercials they had viewed. These people were chosen for the focus groups based upon the opinion of an ASI moderator that they would be willing to discuss their opinions of the commercials they viewed (Seltzer, CX 811G). The ASI moderators who conducted these discussion groups were experienced and highly qualified (Seltzer, CX 811G). The focus group discussion transcript was recorded verbatim with only nonsubstantive editing for readability (*e.g.*, CX 254, Z008-017), and was included in the final ASI report. ASI offers five different services for clients regarding the focus groups, including transcripts, analyses, and tape recordings of the sessions (Seltzer, CX 811H).

193. ASI's audience recruitment procedures are designed to produce a sample that fairly reflects a cross-section of the population in the recruited metropolitan areas. From each of the sampling points, the desired quota of respondents in each age and sex group is selected, i.e., audiences consist of approximately 50/50 sex distribution, and approximately half of the respondents are below age 35, half are 35 or older (Seltzer, CX 8IIB). Further, two separate selection procedures are used for each audience. Some viewers are recruited through personal contacts at high-traffic locations, such as shopping centers, in an effort to secure a sample that reflects the differing geographic and socio-economic characteristics within that metropolitan area (Seltzer, CX 8IIB). Others are selected via telephone, using a "reverse directory" system. Reverse directories list telephone numbers by street addresses rather than names so that ASI can secure a geographic balance among the respondents recruited by telephone (Seltzer, CX 8IIB-C).

194. The questionnaires, as can be seen from examining the 17 reports in evidence, are designed to be self-administered by members of the general public (see, *e.g.*, CX 245Z104-12). They consist of simple multiple-choice questions, and equally simple open-ended recall questions. In order that the testing be run smoothly, ASI's theater operation employs only highly qualified individuals, and it trains them extensively (Seltzer, CX 8IIG).

195. Responses to the open-ended questions in the questionnaires were coded internally by ASI's coding department, which was adequately staffed, experienced and qualified (Seltzer, CX 8IIH-I). Both the supervisor and assistants checked the accuracy of coding and resolved possible coding problems (Seltzer, CX 8IIH). Coding of responses to both the "main idea of the commercial" and the "recall" questions (see, *e.g.*, CX 254Z028, 031) included the preparation of a recommended coding outline for each question, based upon established criteria, which was approved by the coding supervisor and then by the project director (Seltzer, CX 8III). Whenever possible, ASI used the same codes in testing a particular product over a period of time for comparisons across tests. After the project

director approved the outline, the coder coded each verbatim comment. The accuracy of coding was checked first by the coding supervisor, and second by the project director's assistant if a problem arose which warranted it (Seltzer, CX 811I).

196. Coded open-ended responses together with closed-ended (or "check off" type) responses were keypunched twice by ASI's internal keypunching department to ensure accuracy. Then they were processed by a computer. Keypunchers were experienced and qualified (Seltzer, CX 811I). The computer printouts of coded responses which followed keypunching were checked three times: by the coding supervisor, the project director and by the editing department (Seltzer, CX 811J). The printouts were checked by the computer operator before they were released from that department to a project director. The project director reviewed and analyzed the computer output presented, and approved the form of its presentation in the final report. These draft final reports were sent to the editing department for final checking before a senior ASI employee (a Research Unit Director or a V.P. Research) examined the final document (Seltzer, CX 811J-K). Verbatim audience comments (see, *e.g.*, CX 246) were transferred by typists from the original questionnaires. ASI's procedures permitted corrections for only obvious spelling errors, but no changes in wording (Seltzer, CX 811K). After the reports were completed (CX 245, 246, 249-259; CX 261-264) by the ASI office in Los Angeles, they were sent to both the client and to that product's account executive in ASI's New York office (Seltzer, CX 811K).

2. *Copy Tests Prepared by Ted Bates*

197. Five copy tests received into evidence (CX 267, 268, 269, 270, 271) are reports prepared by Ted Bates & Company of copy tests performed on various Bufferin television advertisements. Except for CX 271, these copy tests were performed between February 1968 and May 1969, according to a method developed by Bates called "The Copy Lab" (Jack, Tr. 6089).

198. Anne Jack[5], a former Vice President of Ted Bates and Company, testified for complaint counsel concerning the design and general procedures, as well as the mechanics of conducting these tests.

199. "Copy Lab" testing was based on the use of uniform methods of recruiting, questioning of respondents and reporting of results in all studies (Jack, Tr. 6089). When Bates determined to "Copy Lab" test the advertisements reflected in the above-mentioned reports, it contacted Graham Research, an independent contractor, and advised it of that determination. Bates then supplied this independent contractor with films of the advertisements to be tested, the questionnaires to be administered, specifications for the size of the sample, and recruiting quotas in terms of age, sex and education (*e.g.*, the "Copy Lab" sex quota specified 100 percent women) (Jack, Tr. 6089-90). With complete instructions, the independent contractor implemented the "Copy Lab" procedures. First, they positioned a specially designed trailer in a shopping center in New York or New Jersey. From the shopping center, Graham recruited customers who, if they fit within the recruiting quotas above mentioned, were invited to enter the trailer and participate in the test (Jack, Tr. 6090).

200. A preliminary questionnaire was administered to respondents (see, *e.g.*, CX 299T-W). After filling out the preliminary questionnaire, respondents were shown a short film strip which contained one advertisement at the beginning, one at the middle and one at the end (Jack, Tr. 6090). Five-minute entertainment segments were interspersed between the three advertisements. The order of presentation of the three advertisements was rotated so that each appeared first, second and third, an equal number of times (Jack, Tr. 6091).

201. Immediately after the respondents viewed the material, they received another questionnaire which asked, first, their recall of various elements of the three advertisements they viewed; second, their comments about the Bufferin advertisements in particular; and third, their intentions to purchase var-

5 Anne Jack is the former Anne Weitz. Her name appears as Weitz in this document to reflect testimony or documents which identify her as Ms. Weitz.

ious brands (see, *e.g.*, CX 299X-Z003; except that the question appearing at page Z003 was not a part of standard "Copy Lab" procedure) (Jack, Tr. 6091).

202. Graham submitted the completed questionnaires directly to Bates without editing or coding any of the responses (Jack, Tr. 6091). Upon receipt of the completed questionnaires, Bates first checked for adherence to quota requirements and for general completeness. A Bates secretary retyped respondents' answers to the immediate recall open-ended questions (see, *e.g.*, CX 299Y) with no editing and at most corrections of obvious spelling errors.

203. Bates employees coded and tabulated respondents' answers to these open-ended recall questions. Bates typed verbatim responses, and the tables of coded responses to the open-ended recall questions were among other information included in a report of standardized format (Jack, Tr. 6092). Such reports were prepared by Bates and were submitted to Bates' Bufferin account management for review.

204. Under certain circumstances, Bates determined to copy test a particular advertisement by a less time consuming method. One manner of effecting an expedited test was to employ a system called the "Quick Copy Lab" (Jack, Tr. 6092). CX 229, 300 and 301 reflect the results of "Quick Copy Lab" tests of certain advertisements (Jack, Tr. 6092).

205. The difference in methodology between the "Copy Lab" and "Quick Copy Lab" systems centered in the area of respondent recruiting. Rather than stationing a trailer in a shopping center and recruiting respondents individually according to preset quotas (F. 119, *supra*), Bates instructed the independent contractor to recruit respondents in groups according to general age and education ranges, *e.g.*, organized clubs or other groups of consumers recruited as a whole. "Copy Lab" and "Quick Copy Lab" systems differed also in the location at which the materials described (F. 200, *supra*) were viewed. Rather than a mobile trailer which could accommodate only three to four viewers at a time, respondents in "Quick Copy Lab" reviewed the materials in a central loca-

tion which could accommodate 25 to 30 people (Jack, Tr. 6093). Except for CX 301, the questionnaires administered in "Quick Copy Lab" were the same as those used in "Copy Lab" tests. The procedures for forwarding completed questionnaires to Bates and Bates' use of those questionnaires were also the same. Reports of the standardized format used in "Copy Lab" were not prepared for "Quick Copy Lab" tests (Jack, Tr. 6093), 206. With respect to CX 301, the questionnaire administered contained questions in addition to the standard individual recall/purchase interest questions. These questions asked about respondents' identification with and belief in the person featured in the advertisement and were designed to determine respondents' own experience with arthritis (Jack, Tr. 6093-94). Upon completion these questionnaires were sent for coding to Action Research, a subsidiary of Bates located in Universal City, California. The tabulations of coded responses to the questionnaires and the completed questionnaires were then forwarded to Bates, where CX 301 was then prepared. The typed verbatim responses appearing at CX 301Z016-044 differ from the other Bates copy tests in that these report not only the responses to the standard open-ended recall questions (see, *e.g.*, CX 299Y-Z), but they also report answers to a question regarding reaction to the commercial. The precise wording of this latter question is not known, but it appears to have been worded as the corresponding question in CX 299Z003 (Jack, Tr. 6094).

3. *Copy Tests by H.D. Ostberg Associates*

207. Six copy tests in evidence (CX 271, 285, 286, 288, 289, 290) (Ostberg copy tests) are reports of copy tests conducted by H.D. Ostberg Associates on various Bufferin and Excedrin television advertisements involved in this proceeding (Ostberg copy tests). Henry Ostberg testified for complaint counsel regarding the conduct and reporting of these tests, which his company performed for the respondents.

208. At the time these tests were conducted, Mr. Ostberg was the owner and President of H.D. Ostberg Associates. This company is now a division of the Admar Research Company,

of which Mr. Ostberg is Chairman of the Board (Ostberg, Tr. 4449-54). Admar Research provides services in marketing and advertising research and consulting (Ostberg, Tr. 4450). Certified Surveys, another company owned by Mr. Ostberg at the time these copy tests were conducted, is a field work and tabulation firm which, through retained independent contractors, supervised, collected, and tabulated the data of each test, but performed no analysis of the data. Currently, Certified Surveys is the company which conducts most of the field work for Admar Research (Ostberg, Tr. 4454-55). In addition to founding Admar Research and its predecessors, Mr. Ostberg's background includes a professorship in Marketing at the New York University for nine years, a law degree from the New York Law School, a Master's degree in Business Administration and a Ph.D. from Ohio State University (Ostberg, Tr. 4450). Ostberg Associates' clients have included Admar, Bristol-Myers, Lever Brothers Company, Miller Brewing Company, Philip-Morris, Nabisco, IBM, and BASF. For Bristol-Myers, Mr. Ostberg has conducted copy tests and tracking studies from 1965 to the present in various product categories, including OTC analgesics (Bufferin, Excedrin), deodorants, suntan lotions, and men's hair preparations. He also served as a consultant for Bristol-Myers in this proceeding (Ostberg, Tr. 4455-58). Mr. Ostberg's clients are generally advertisers, but he sometimes serves his client's advertising agency in an ancillary role, assisting in its preparation of marketing and advertising research for the client (Ostberg, Tr. 4456-57). He has also conducted studies for Young & Rubicam where the client was Bristol-Myers (Ostberg, Tr. 4457).

209. Bristol-Myers first requested Mr. Ostberg to perform copy tests of Bufferin and Excedrin advertisements in the late 1960's. Mr. Ostberg collaborated with Dr. Edward Berdy, Director of Marketing Research for Bristol-Myers at that time, in the design, development and pre-testing of the "shopping center van technique" used in the six Ostberg copy tests of Bufferin and Excedrin advertisements in the record.

210. The execution of the copy tests and preparation of test results were directly supervised by senior executives of Admar, who reported directly to Mr. Ostberg (Ostberg, Tr. 4469-70).

211. The copy tests performed by H.D. Ostberg Associates for Bristol-Myers employed the so-called "shopping van technique." According to Mr. Ostberg (Ostberg, Tr. 4480-81) the methodology was as follows: Upon notification to H.D. Ostberg Associates that Bristol-Myers requested the copy testing of an advertisement, employees of independent contractors employed by Certified Surveys were sent to shopping centers in Philadelphia, Chicago, Detroit or Los Angeles to perform the actual tests (Ostberg, Tr. 4461, 4480). These employees would ask shoppers at the shopping center to participate in a television survey, and, if they agreed, have them enter a van equipped with a motion picture projector located at the shopping center. The shoppers were then asked a set of preliminary questions regarding product usage and preference (see, *e.g.*, CX 290Z022-023). Those shoppers who indicated that they used an analgesic were then shown a travelogue, including several advertisements, among which were the commercials to be tested. Afterwards, the shoppers were presented with an opportunity to select a discount coupon for one of several products in several different product categories. The shoppers then left the van. Within 24 hours the shoppers were telephoned by independent contractors of H.D. Ostberg Associates and asked recall questions about the commercial they had viewed the previous day. According to standard practice, H.D. Ostberg Associates would then perform limited validation to determine the genuineness of the results. The completed questionnaires were forwarded to H.D. Ostberg Associates, where the results were coded, keypunched, and tabulated internally.

212. The results were then put in a tabular format, which was either produced by computer or typed (Ostberg, Tr. 4483). The verbatim responses to recall questions were sometimes also attached (see, *e.g.*, CX 290Z007-Z021).

213. The results were then sent to Bristol-Myers or its advertising agency (Ostberg, Tr. 4484).

214. CX 285 through 290 were produced according to the procedures detailed above (F. 211, *supra*) (Ostberg, Tr. 4513, 4517-19, 4525). CX 271 includes two tables of coded responses bearing the notation "Recoded, ASW" (CX 271J-L). Anne S. Weitz (Jack), a former Vice President of Ted Bates, who testified about CX 271, did not recall the exact circumstances of that notation (Jack, Tr. 6094-95).

215. The ASI Audience Reaction Tests are the most elaborate copy tests in evidence. The ASI copy tests appear to have been used by other advertisers and advertising agencies. Ted Bates' "Copy Lab" and "Quick Copy Lab" copy tests are not as elaborate as the ASI tests. Neither are the Ostberg's "Shopping Van" copy tests. Although these survey results are not technically projectable to any general population or subgroup, the results have been used by advertisers and advertising agencies as a reliable and practical means of gauging likely audience reactions to proposed television advertising copies. In this proceeding, they are reasonably reliable confirmatory evidence on the issue of what a television commercial can reasonably be expected to convey to the viewer.

D. Some Other Documentary Exhibits

1. *The AMA Drug Evaluations*

216. Dr. John Lewis is a pharmacologist, experienced in testing analgesics, who presently holds the position of Senior Scientist in the Department of Drugs of the American Medical Association (Lewis, Tr. 4159-61). Since associating with the AMA in 1960, Dr. Lewis has held a number of positions, each of which has involved supervising the publication by the AMA of monographs evaluating new drugs. Prior to development of the three editions of the *AMA Drug Evaluations*, such monographs were published in the *Journal of the American Medical Association* and the predecessor publication to the *AMA Drug Evaluations*, titled *New and Nonofficial Drugs* (Lewis, Tr.

4163-64). The Council on Drugs, a standing committee of the AMA, reviewed and commented on all material prepared by Dr. Lewis and his staff prior to publication (Lewis, Tr. 4165). The basis for evaluation and review of material published on new drugs included the published literature and unpublished data submitted to the Council by pharmaceutical manufacturers (Lewis, Tr. 4166). In many instances the information was the same as that submitted to FDA with a new drug application (Lewis, Tr. 4166).

217. The American Medical Association published three editions of the *AMA Drug Evaluations*, in 1971, 1973 and 1977. The publication was a comprehensive compilation evaluating all types of drugs available to the medical profession including single entity drugs and mixtures (Lewis, Tr. 4167). Virtually all of the drugs in the U.S. Pharmacopoeia and the National Formulary as well as 500 of the most commonly prescribed drugs were included in the evaluation (Lewis, Tr. 4170). The evaluations were based on all of the available information including published and unpublished work made available to the AMA and the advice and opinions of consultants, and the AMA's Council on Drugs (Lewis, Tr. 4171). Information in the book includes the nonproprietary name of the drug, trade names, action and uses of the drug, comparative safety and efficacy, significant adverse reactions, precautions, preparations available, and the manufacturer's name (Lewis, Tr. 4171).

218. The Council on Drugs of the AMA was comprised of 12 members, appointed by the AMA Board of Trustees for their expertise in the area of drugs, and was responsible for overseeing publication of the *Drug Evaluations* (Lewis, Tr. 4172). Two of the members of the Council — Drs. Wood and Adriani — were recognized experts in the field of analgesics, both having done considerable research and publishing in the field (Lewis, Tr. 4173). The Council chairman appointed an Ad Hoc Committee to review initial material submitted by staff and to make comments and suggestions on each chapter (Lewis, Tr. 4174). The Ad Hoc Committee included Dr. Alan Bass, Chairman of the Department of Pharmacology at

Vanderbilt University, Dr. Daniel Rogers, a practicing physician, and the Council Chairman, Dr. Adriani. Draft chapters were also sent to outside consultants for their comments. For the first edition of the *Drug Evaluations*, the outside consultants asked to comment were chosen by staff of the Council on Drugs. Dr. William Beaver was among the outside consultants contacted for review of the first edition (Lewis, Tr. 4175-76). The Council member assigned to review the first edition's chapter on mild analgesics (CX 518) was Dr. Lauren Woods, an eminent authority in analgesics who is presently Vice-President for Health Affairs at the Medical College of Virginia and previously chairman of the Department of Pharmacology at University of Iowa Medical School (Lewis, Tr. 4177).

219. A revised copy of the Mild Analgesics chapter incorporating comments of consultants was reviewed and commented upon by Dr. Woods. His comments were then submitted to the Associate Director of the Department of Drugs and the Secretary to the Council on Drugs, Dr. Lewis, who considered comments and incorporated them into a revised chapter before it was submitted to the Ad Hoc Committee of the AMA's Council of Drugs. The final proof of the first edition of the book was commented upon by the Pharmaceutical Manufacturer's Association, who had requested an opportunity to review it. Errata sheets were included with the first edition to reflect necessary changes in keeping with those comments (Lewis, Tr. 4179). Approximately 165,000 copies of the first edition of the *Drug Evaluations* were distributed to all members of the American Medical Association and another 40,000 were sold (Lewis, Tr. 4179-80).

220. In preparing the chapter on Mild Analgesics (CX 512) for the second edition (1973) of the *Drug Evaluations*, an initial draft was prepared based on the first edition and then submitted to Dr. Lauren Woods for review and comment. A revised draft incorporating his comments was prepared by Dr. Lewis and his staff and then submitted to outside consultants (Lewis, Tr. 4182). The consultants who received copies of this edition were Dr. William Beaver, Dr. Abraham Sunshine, Dr. Louis Lasagna and Dr. Dixon Woodbury. Replies were re-

ceived from Dr. Sunshine and Dr. Woodbury (Lewis, Tr. 4182). These comments were carefully reviewed and another revised draft was prepared for Dr. Woods and the Committee of the Council on Drugs. That Committee was not the same Ad Hoc Committee which reviewed the chapter for the first edition, but had more members, including former Ad Hoc Committee member Dr. L. Paulson, an expert in endocrinology and a Professor of Medicine at the University of Washington, and Dr. Daniel Azarnoff, Professor of Medicine and Clinical Pharmacology at the University of Kansas Medical School, who reviewed the chapter (Lewis, Tr. 4189; Azarnoff, Tr. 9196-98).

221. A revised draft of the chapter on Mild Analgesics was also sent to drug manufacturers, including Bristol-Myers (Lewis, Tr. 4184-85). Comments were referred to Dr. Woods for his opinion and advice (Lewis, Tr. 4188).

222. A final revision of the chapter was sent to the publisher after Dr. Woods reviewed the comments (Lewis, Tr. 4188). Approximately 65,000 copies of the second edition were sold (Lewis, Tr. 4189).

223. Complaint counsel's experts have attested to the reputation and reliability of the *AMA Drug Evaluations* as a source for conclusions about the safety and efficacy of drugs used by physicians (Azarnoff, Tr. 9197-98; Moertel, Tr. 5634).

2. *The Medical Letter*

224. The *Medical Letter* was founded in 1969 to provide physicians with an unbiased source of scientific information about drugs. It is an independent publication that does not sustain itself through advertising or affiliation with any manufacturers (Abramowicz, Tr. 2712). The *Medical Letter* now has over 107,000 subscribers, most of whom are physicians (Abramowicz, Tr. 2720). The *Medical Letter* is structured with both an editorial board and an advisory editorial board. The editorial board is comprised of an editor, Mark Abramowicz, M.D., and two associate editors who are lay science writers. The advisory editorial board is composed en-

tirely of physicians who are selected on the basis of their qualifications and expertise in various fields of medicine (Abramowicz, Tr. 2713-14).

225. Articles that are published in the *Medical Letter* first go through a peer review process. Proposed articles are first reviewed by the editor and then sent to the editorial board for comment. Drafts are also sent to the members of the advisory editorial board for their comments. In addition, it is the practice of the *Medical Letter* to have all drafts reviewed by outside consultants who have special expertise in the subject matter of the proposed article. A proposed article is usually reviewed by at least six to eight outside consultants, but on some occasion it may be reviewed by as many as 60 outside experts. Proposed articles are also sent to the senior authors of the articles cited in the draft and to the manufacturer of the drug the article involves. Drafts are also routinely sent to governmental agencies such as the Food and Drug Administration and the United States Pharmacopoeia (Abramowicz, Tr. 2714-16).

226. The *Medical Letter*'s editorial staff also prepares a bibliography and reviews current literature for each proposed article. This process is calculated to ensure the accuracy of the statements made in the articles that appear (Abramowicz, Tr. 2219). Final articles that appear in the *Medical Letter* incorporate the comments and corrections made as a result of this extensive review process (Abramowicz, Tr. 2718). This review process was followed in the development of CX 510, the July 5, 1974 issue of the publication titled "Is All Aspirin Alike?" (Abramowicz, Tr. 2727-33). Dr. Gehrard Levy, an expert in pharmacokinetics (Lanman, Tr. 11660-61; Abramowicz, Tr. 2733) and a consultant to Bristol-Myers in this matter (Tr. 8991-92), was a member of the advisory editorial board of the *Medical Letter* and personally participated in the development of CX 510 (Abramowicz, Tr. 2733).

227. Because of the peer review process by highly qualified experts in the field and the thorough check for accuracy, the *Medical Letter* is a highly reliable source of information about

the opinion of experts regarding the safety and efficacy of drugs. Two of complaint counsel's expert witnesses attested to the reliability of the *Medical Letter* for that purpose (Moertel, Tr. 5631-32; Azarnoff, Tr. 9198-99).

228. The *AMA Drug Evaluation* chapter on mild analgesics (CX 512) and the Medical Letter article "Is All Aspirin Alike?" (CX 511) were received in evidence for the limited purpose of corroborating other evidence in the record by showing that these publications expressed views in accord with the opinions of expert witnesses who testified for complaint counsel regarding common issues.

IV.

Respondents' Advertisements Made The Representations Alleged In the Complaint

A. Representations: Applicable Standards

229. The standard for determining the meaning of an advertisement is whether, from an examination of the advertisement as a whole, an interpretation is reasonable in light of the claims made therein. The Commission or an administrative law judge may determine the meaning of an advertisement solely from an examination of what is contained therein, without consumer testimony or survey data regarding how consumers in fact perceived the advertisement.

230. In addition, the Commission or an administrative law judge may, where appropriate, consider other testimonial and empirical evidence as an aid in determining the meaning of an advertisement. The record contains the opinion testimony of Dr. Ross and reports of copy tests which were conducted on certain advertisements in evidence and certain consumer research. The so-called penetration studies generally are not designed to ascertain how certain consumers perceive the meaning of advertisements: their emphasis is on consumer recall.

Expert Opinion Testimony

231. In reaching his expert opinion as to whether the representations alleged in the complaint were made in advertising for Bufferin, Excedrin and Excedrin P.M., Dr. Ross employed appropriate standards (Ross, Tr. 6944, 8169-71). Dr. Ross based his conclusions as to whether the challenged advertisements could reasonably have been understood by consumers on his experience with consumers, adopting their frame of reference which included, indirectly, their background or prior experience (Ross, Tr. 8185). Dr. Ross' judgments as to the representations made in challenged advertising for Bufferin, Excedrin and Excedrin P.M. were his independent expert opinions and were reached without reference to or reliance on data contained in copy tests, penetration studies or image studies (Ross, Tr. 6944-46).

232. However, Dr. Ross did refer to examples of supporting or confirmatory evidence that there were consumers who perceived or understood television advertisements as meaning, saying or showing certain of the alleged representations. Such confirmation or support was in the form of verbatim comments in copy tests which were elicited in response to comprehension and/or recall questions, and in the form of transcripts of focus group discussions (Ross, Tr. 6946). Dr. Ross prepared CX 815, 817, and 820 which list the representations that the complaint in this matter alleges were made in advertisements for Bufferin, Excedrin and Excedrin P.M. respectively (Ross, Tr. 6943). He also prepared CX 816, 818 and 821 which reflect his evaluation of and testimony as to whether the alleged representations were made in the challenged advertisements (Ross, Tr. 6957). Also indicated on these matrices are the exhibit numbers of copy tests which were run on specific advertisements which were made available to Dr. Ross for his review (Ross, Tr. 6959).

B. The Bufferin Advertisements In Evidence Make The Challenged Representations

1. *Core Representations*

a. *Complaint Paragraphs 9(A)(1) and 9(A)(2)*

233. Bristol-Myers has represented that Bufferin relieves pain faster than aspirin relieves pain (Complaint Paragraph 9(A)(1) and that Bufferin relieves pain twice as fast as aspirin relieves pain (Complaint Paragraph 9(A)(2). The ''faster than aspirin'' claim is contained in CX 1-19, 22-46, 61-98, 100, 101, 103-105, 107, 109-114, 717D-G, 719-21, 671S, T, V, W, Z018-20. The ''twice as fast'' claim is contained in CX 1-19, 22-46, 48, 49, 52-60, 61-98, 100, 101, 103-105, 107, 109-113, 719, 720, 721, 717D-G. Bristol-Myers has admitted that they represented through advertisements that Bufferin relieves pain faster than ''plain'' or ''simple'' aspirin relieves pain. (Answer of Bristol-Myers Company, Paragraph 7; Answer of Bates, Paragraph 9).

234. The fact that this representation, as alleged in Paragraph 9(A)(1), was made is shown by the advertisements themselves and confirmed by expert testimony (see CX 815, CX 816A-C; Ross, Tr. 6960-76). Confirmatory evidence is also found in the following copy tests: CX 245, 246, 249, 250, 251, 267, 268, 269, 270, 272, 299, 300, 301.

235. This representation was made wherever the ''twice as fast claim was made because ''twice as fast'' is merely a more extreme version of the same speed claim (Ross, Tr. 6960). In addition, the representation was made in the following advertisements which depict a tense situation where, ''[P]lain aspirin's fine, but Bufferin goes to work much faster,'' CX 51A. (See also, for similar language CX 48, 49, 52, 53, 54, 55, 56, 57, 58, 59, 60.)

236. The advertisements cited in F. 233, *supra*, made the representation alleged in Paragraph 9(A)(1) because consumers would have understood them as representing that Bufferin

relieves pain faster than aspirin. This understanding of the advertisements reflects two factors: (1) that consumers understand "goes to work faster" as meaning Bufferin relieves pain faster (Ross, Tr. 6963), not merely that Bufferin gets into the bloodstream faster, and (2) that consumers understand "plain" or "simple" aspirin to mean "aspirin." This understanding of the advertisements is confirmed by documentary evidence provided by comments in copy tests run on a number of different advertisements. With respect to the interpretation of "goes to work faster," viewers were asked what "how long it takes to go to work" means (CX 272). Given a choice of three alternatives, including "to get into the bloodstream," the majority chose "for your headache to start feeling better" (CX 272T; Ross, Tr. 6963). In a focus group discussion run by A.S.I., the group was asked what was being referred to by "half the time." The response was, "From the time you take the product to the time you're relived of your headache . . . comparing it to aspirin or anybody else's product" (CX 245Z044). Recall of one advertisement, CX 82a, again shows that in comments related to speed, respondents said Bufferin "gets to your head/headache faster" (CX 250P, see also 251P for same results on a different advertisement, CX 74a). Verbatim comments on an advertisement where the "faster" claim is made, independent of the "twice as fast claim" (CX 53a), further support the fact that consumers equate "goes to work faster," with faster relief of pain. In responding to the question, "What was said about the brand," viewers said, "Better than aspirin, works faster to kill pain" (CX 299H, respondent 3), "Relieves headaches fast" (CX 299H, respondent 6), "Quicker relief" (CX 299I, respondent 19), and "Fast acting pain relief" (CX 299J, respondent 27). In a copy test run on another advertisement (CX 22a), respondents clearly understood the speed claim as referring to relief, "Gets headache better in half the time" (CX 267W, respondent 85), ". . . Bufferin cuts the time in half to reach the pain," (CX 267W, respondent 86), "Bufferin relieves in half the time," (CX 267W, respondent 88).

237. The fact that consumers understand the reference to "plain" or "simple" aspirin as a reference to "aspirin" as alleged in Paragraph 9(A)(1), is also reflected in the focus group discussions and verbatims. A number of the comments cited above refer specifically to "aspirin." Other verbatims which support this include the following: "Works twice as fast as aspirin" (CX 269Z003, respondent 125). Based on these verbatims it is reasonable to conclude that the representation as alleged in Paragraph 9(A)(1) was made and that the admission by respondents that they represented that Bufferin relieves pain faster than "plain" or "simple" aspirin (see F. 233, *supra*) is an admission that the representation as alleged was made.

238. The fact that Bufferin advertisements made the alleged representation in Paragraph 9(A)(2) is demonstrated by the advertisements themselves and by expert testimony (Ross, Tr. 6960, 6965-68). This representation was made through a variety of express and implied claims concerning Bufferin's ability to relieve pain twice as fast as aspirin and through the use of various audio/visual techniques:

(a) A close-up focusing on language in the Bufferin label which reads "Twice as fast as aspirin." (Ross, 6965, see CX 1-7, 22-23, 26, 27-28, 29-31,34-35, 43-44, 61A, 64A-67, 73-75, 85, 90, 98, 99, 100-101, 103-114).

(b) A picture of one-half of the face of a clock or watch is shown accompanied by language such as:
"Bufferin can cut the waiting time in half. Half the time. That's Bufferin time."
(CX 25, see also CX 1, 22, 23, 26, 27-28, 29, 31, 33; Ross, Tr. 6967).

(c) Anncr: "In the first important 30 minutes Bufferin delivers twice as much pure pain reliever as the best known aspirin. Twice as much." (Ross, Tr. 6965; CX 3A; for similar language see also CX 2, 4, 7, 10, 12-13, 15, 22-24, 26, 27-28, 29, 30-38, 61, 63-64, 67, 99).

(d) "Bufferin goes to work in half the time." (Ross, Tr. 6967; CX 1, 23, 24, 25, 26, 27-39).

(e) Certain graphic techniques make this representation without any direct literal or audio referance to the "twice as fast" claim. One of the techniques shows a computer typewriter printing out two columns, one "aspirin," the other BUFFERIN." The "aspirin" column is printed out more slowly and ends up being about half the size of the "BUFFERIN" column. The image is one of speed, which is reflected in the height which the columns reach in the same time ("Bufferin reaches its height twice as fast") and enhanced by the use of a special computer typewriter which prints faster than an ordinary typewriter. (See CX 2-4, 7, 61, 63, 64, 67). Another technique uses the image of a tablet of aspirin and a tablet of Bufferin disintegrating, the particles of each moving from the stomach of an anatomical model, to its head. Twice as much of the Bufferin has disintegrated as the aspirin. The technique is used in both print and film advertisements and represents that the faster acting Bufferin is twice as fast as aspirin (CX 68-77, 82-84, 109-110). Finally, this effect is also achieved in the series of advertisements which show two whole Bufferin tablets in a circle with two half-tablets of aspirin. The announcer is shown moving both Bufferin tablets out of the circle and into another one representing headache relief while the aspirin tablets remain inside the first circle (CX 9-15). The graphic 2:1 comparison is thus another means of representing that Bufferin is twice as fast as aspirin.

239. The advertisements cited in F. 238 (a-d), *supra*, made the representation alleged in Paragraph 9(A)(2) because consumers would have understood their comparative speed claims as representing that Bufferin relieves pain twice as fast as aspirin relieves pain (Ross, Tr. 6961-63, 6965). This perception by consumers, tying Bufferin's speed claim to onset of pain relief

is evidence in the verbatims of copy tests and in focus group discussions associated with these advertisements which repeatedly play back that consumers' understanding of these claims in the context of the amount of time it would take for them to perceive relief from headache pain. Confirmatory evidence supporting the allegation in Paragraph 9(A)(2) is contained in the following copy tests: CX 245, 246, 249, 250, 251, 267, 268, 269, 270, 272, 300, 301. The following examples from available copy test results supply evidence of how consumers understood the graphic techniques described in F. 238 (a), (b), (d) and (e):

(a) "Relieved pain twice as fast as aspirin" (CX 301Z017, respondent 7, see also respondents 20, 21, 26, 27, 29, 32).

(b) Cut headache time in half by using Bufferin which works twice as fast" (CX 267V, respondent 75), ". . . spoke about quickness that Bufferin gave in headache relief . . . cut time in half" (CX 267S, respondent 237); "Bufferin relieves you of a headache in half the time" (CX 270Z006, respondent 21).

(d) See discussion at F. 236, *supra*, which explains that consumers understood the "goes to work faster" claim as referring to speed of onset of *pain relief*.

(e) In response to a question regarding recall of what was seen in an advertisement using the computer-typewriter graphic, the following comments were made: ". . . and a diagram of how much faster it works than plain aspirin" (CX 301Z016, respondent 2); "typedwritten [sic] words for aspirin [sic] and bufferin with bufferin in the lead for fast action in the stomach" (CX 301Z019, respondent 22).

In describing what was seen in those ads where Bufferin was shown rushing to the headache of an anatomical figure, these comments were made:

"It's twice as fast as aspirin because most of the dose goes immediately to the head and relieves the headache while aspirin stays in the stomach longer" (CX 300M, respondent 86).

b. *Complaint Paragraphs 9(A)(4) and 9(A)(5)*

240. Bristol-Myers has represented that Bufferin will not upset a person's stomach (Complaint 9(A)(4) and that Bufferin will upset a person's stomach less frequently than aspirin (Complaint 9(A)(5). The absolute "no stomach upset" claim was made in the following Bufferin advertisements: (a) CX 2-7, 11, 17, 19A, 40-41, 42A-46, 61A-64A, 93-98, 105, 717F. The "less frequent upset" claim was made in: (b) 2-7, 11, 17, 19, 40-41, 43-46, 49, 715, 52-56, 61A-91, 96, 97, 109-112, 114, 717F, 719-721.

241. Bristol-Myers admitted representing through the challenged advertisements that Bufferin will cause upset stomachs less frequently than plain or simple aspirin (Answer of Bristol-Myers Company, Paragraph 7, Answer of Bates, Paragraph 9). This is a clear admission that Bufferin advertisements cited above made the representation as alleged in Paragraph 9 (A)(5). This is confirmed by expert testimony (Ross, Tr. 6982-85; CX 815, CX 816) and verbatim comments contained in the following copy tests: CX 249, 250, 251, 299, 300, 301.

242. The fact that the "less frequent upset" representation was made is confirmed by verbatims from copy tests. For example: "Doesn't upset your stomach like plain aspirin," (CX 31Z016, respondent 2); ". . . and doesn't leave stomach upset as aspirin sometimes does," (CX 301Z019, respondent 22); "Does not upset your stomach like ordinary aspirin," (CX 301Z035, respondent 15); ". . . without upsetting stomach like plain aspirin." (CX 301Z037, respondent 27); "Doesn't have ill effect on stomach like aspirin," (CX 301Z038, respondent 33); ". . . does not upset your stomach the way aspirin does," (CX 301Z042, respondent 73); "Less upset stomach," (CX 300F, respondent 140); ". . . reaches your head pain with less upset stomach . . .," CX 300F, respondent 141); "Less stomach distress," (CX 300F, respondent 46); "It

is milder for the stomach," (CX 299J, respondent 25); ". . . more gentle and more effective than any other brand," (CX 299M, respondent 55). Based on these verbatims, expert testimony and respondents' admissions, it is reasonable to conclude that the representation as alleged in Paragraph 9(A)(5) was made.

243. The fact that Bufferin advertisements made the "no upset" representation in Paragraph 9(A)(4) is demonstrated by the advertisements themselves, and confirmed by expert testimony (Ross, Tr. 6983-85; CX 815, CX 816). Further confirmatory evidence is contained in the following copy tests: CX 300, 301.

244. These representations were made through a variety of express and implied statements making absolute, noncomparative claims which convey the message that Bufferin does not cause stomach upset. Bufferin's special quality of gentleness to the stomach is made through a noncomparative assertion which is communicated simultaneously with a comparative claim (Complaint ¶ 9(A)(5)):

(a) "Bufferin doesn't upset my stomach, the way plain aspirin sometimes did" (CX 3) (See also CX 2, 4-7, 40-41, 43 and 66 for similar language.)

(b) "Bufferin gives more of the pure pain reliever going against the headache. More pure pain reliever, faster than plain aspirin. *Without the stomach upset* plain aspirin can cause" (CX 11, emphasis added). See also, for similar language, CX 17, 19, 44, 45-46.

(c) "Special ingredients in Bufferin lets you take it 4, 5, 6 times a day *without fear of stomach distress* plain aspirin can often cause" (CX 96, emphasis added).

(d) "Bufferin is marvelous. And it doesn't upset my stomach the way plain aspirin sometimes did. ANNCR: (VO) Every single Bufferin analgesic tablet contains gentle antacids *specifically made to help*

prevent the stomach upset that plain aspirin can cause'' (CX 67, emphasis added).

245. The advertisements cited above made the representation alleged in Paragraph 9(A)(4) because consumers would have understood them as representing that whether because of special ingredients, faster dissolution or antacids, Bufferin will not upset a person's stomach (Ross, Tr. 6982).

246. The fact that consumers understood these advertisements as making the absolute ''no stomach upset'' claim as alleged in Paragraph 9(A)(4) is repeatedly played back in copy tests run on some of the advertisements cited in F. 240(a), *supra*. For example: ''Doesn't upset stomach,'' (CX 301Z016, respondent 1); ''Relieves pain — no upset stomach — . . .,'' (CX 301Z016, respondent 3; see also respondents 1, 2, 4, 6, CX 301Z016; respondents 5, 11, CX 301Z017; respondents 14, 20, CX 301Z018 for similar language).

c. *Complaint Paragraph 12(A)*

247. Bristol-Myers has represented that Bufferin relieves nervous tension, anxiety and irritability and will enable persons to cope with the ordinary stresses of everyday life (Complaint ¶ 12(A)). These representations were made in the following Bufferin advertisements: CX 715, 48-49, 52-60 (tension relief ads).

248. The fact that the representations were made is evidenced by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 6985-90, 8212-14, 8216, 8219, 8222, 8224-25, CX 815, CX 816). Further confirmatory evidence is also contained in copy test CX 299.

249. These representations were made through a variety of express and implied statement characterizing Bufferin as the drug of choice for relief in situations that produce tension, stress or anxiety. In certain of the cited advertisements, Bufferin is represented as having the ability to affect mood, whether it be to reduce stress, ease irritability or lessen tension. That effect is represented as one separate from relief of pain or headache pain and is generally conveyed, not literally,

but rather by depicting a tense situation, relief from which is obtained after taking Bufferin (Ross, Tr. 6987). For example: (a) An angry student bangs on college professor's desk insisting that the college must change. Professor, trying to keep cool, suggests a meeting. "ANNCR: Often, people who are sensitive to others can be more sensitive to headache pain." [focus on aggravated professor] "Bufferin is for these people. It's strong medicine that treats you gently. . ." (CX 53). (b) With no voice-over, an ad shows Urban Relocation Department worker driving to home of two elderly people to tell them they are going to have to move. Announcer breaks in: "What you have to tell them isn't easy. Not for you. Often people who are sensitive to others, can be more sensitive to headache pain. They want all the help they can get as quickly as possible. [Man, obviously upset, shown taking Bufferin.] Bufferin is for these people. Man informs tenants of the news and announcer breaks in, "Bufferin. For sensitive people. [Super: For sensitive people. Better than aspirin.] It's better than aspirin." (CX 58).

250. It is clear that consumers would have understood the tension relief ads cited above to say that Bufferin can effectively relieve the anxiety or tension which would ordinarily arise in situations like those depicted in the advertisements, apart from Bufferin's ability to relieve pain or headache pain (Ross, Tr. 6987). The dominant theme of the tension relief advertisements is situational tension, not pain or pain relief. This is reflected not only in the text of the ads, but more vividly in the audio/visual portion of the ads (Ross, Tr. 6988, 8222, 8224-25). Thus, consumers would understand Bufferin to be a good tension reliever.

251. This understanding of the advertisement by consumers is confirmed by the verbatim comments in copy tests done on Bufferin advertisements where respondents repeatedly play back the fact that they understand the claim in the context of tension/stress relief, independent of headache relief. Typical of their comments on CX 53A, a tension relief ad, as reflected in CX 299 are: "Relieves tension and headache," (CX 299J, respondent 26); "Young Dean pressured with student demand

grabs a bottle of Bufferin to relief [sic] his tension," (CX 299J, respondent 28); "Relieves pain fast — also relieves tension," (CX 299M, respondent 54); "Helps calm nerves and tension," (CX 299M, respondent 59); ". . . Then the Dean took Bufferin to calm down, (CX 299I, respondent 14); ". . . Bufferin not only relaxed but helped the pain of headache," (CX 299K, respondent 24); "Take a Bufferin, calm down and then make decisions," (CX 299L, respondent 49); "Man under tension taking pills to relieve some," (CX 299N, respondent 69).

252. In certain advertisements, the tension theme, though less dominant, is still obvious (CX 32, 33, 37, 39). This perception by consumers was sometimes reflected in verbatims of copy tests run on some of those advertisements (*e.g.*, CX 270). In an ad entitled "Dinner Party" (CX 32, 33), the hostess is shown amidst her guests who are enjoying themselves while she is shown, hand to head, saying "What a time for a headache." One respondent characterized her as being struck with a headache at a "very important social situation," (CX 270W, respondent 14) which to many might be an anxiety provoking situation. Other, more specific comments include: "Relieves your headache quickly and relieves tension," (CX 270X, respondent 47); "Woman under stress at party. After taking Bufferin obviously relaxed enjoying herself," (CX 270Z006, respondent 25). Another ad, "Moving Day," (CX 37) portrays what viewers would readily identify as a stressful occasion. In this instance, "Mom" gets a headache as she is supervising the apparently gruff movers. The following verbatim from CX 269, a copy test on that advertisement, reflect that viewers associated Bufferin with tension relief: "Mother takes Bufferin for headache and tension," (CX 269V, respondent 27); "Woman in distress at moving time. Saw her take Bufferin and return to happy woman," (CX 269X, respondent 52); "Woman frantic . . . now refreshed after taking Bufferin," (CX 269X, respondent 53); Lady said she was very upset and needed something to take for upset," (CX 269Z002, respondent 104). Another stressful situation appears

in CX 39, "Beauty Parlor," where a hairdresser gets a headache in the midst of her busy work schedule but is relieved after taking Bufferin. Again, the tension theme is not dominant, but is clearly suggested and it is reasonable for viewers to identify with the situation and associate the relief of tension with Bufferin. Therefore, in these advertisements as well as those cited in F. 247, *supra*, respondents have communicated an association between Bufferin and relief from a tense situation.

d. *Complaint Paragraph 17*

253. Bristol-Myers has represented that physicians recommend Bufferin more than any other nonprescription internal analgesic product (Complaint 17). These representations were made in the following Bufferin advertisements: CX 2-7, 41-46, 61, 65-67, 97, 107.

254. The fact that these representations were made is evidenced by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 6994-99; CX 815, CX 816). Further confirmatory evidence is also found in the following copy tests: CX 272, 301.

255. These representations were made through a variety of express and implied statements about the preferences and recommendations of physicians for Bufferin. Bufferin is represented as the brand doctors will specify more than all the leading pain relievers. For example: (a) . . . ANNCR: Of all leading brands of pain reliever you can buy for minor pain, doctors specify Bufferin most [Superimposed on screen: DOCTORS SPECIFY BUFFERIN MOST]. (CX 66). (b) ANNCR: . . . "Doctors specify [super: DOCTORS SPECIFY BUFFERIN MOST] Bufferin most (close-up of super) of all leading brands of headache tablets you can buy. . ." (CX 41).

256. Consumers' understanding that doctors recommend Bufferin is confirmed by verbatim responses included in copy tests on Bufferin advertisements where respondents repeatedly played back the fact that the product was recommended by doctors. For example: "Doctors recommend Bufferin, (CX 301Z042, respondent 58); "Recommended by most doctors for

pain," (CX 301Z037, respondent 24); "It is good to know that there is a product that is actually better for one because a daoctor [sic] sayd [sic] so," (CX 301Z034, respondent 90); ". . . and not harmful to the body — more doctors recommend Bufferin," (CX 272Z, respondent 5); "Works in 1/2 time more doctors recommend it, (CX 272Z001, respondent 19); ". . . recommended more often by doctors . . .," (CX 272Z003, respondent 45).

257. The "doctors recommend" claim expressly compares Bufferin to all *leading brands* of pain reliever. However, the copy test verbatims, not surprisingly, indicate that consumers understood the representation to compare Bufferin to "any other non-prescription analgesic product," *e.g.*, "Doctors recommend it over all pain relievers," (CX 301Z032, respondent 83).

e. *Complaint Paragraph 21*

258. Bristol-Myers has represented that the analgesic ingredient in Bufferin is other than ordinary aspirin (Complaint paragraph 21), and that representation was made in all of the Bufferin advertisements listed in column 14 of CX 816 plus CX 717D-G, 719-21, 761R, S, T, V, W, Z018-20. The fact that Bufferin advertisements made the representation as alleged in Paragraph 21 is shown by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7000-01, 8230-31, 8236-37, 8238; CX 815, CX 816).

259. This representation was made through a variety of express and implied statements consistently positioning Bufferin so as to distinguish it from aspirin and, in fact, to avoid any possible inference that Bufferin contains aspirin (Ross, Tr. 8237). That is, in certain of the advertisements, Bufferin is represented as faster, gentler and able to provide greater pain relief than aspirin by directly comparing Bufferin and aspirin with respect to those qualities (Ross, Tr. 7000-01, 8230). For example: (a) "ANNCR: You have a headache. You've taken aspirin. How long before it . . . goes to work? You should have taken Bufferin. Bufferin . . . can cut the time . . . in half. Half the time. That's Bufferin time. Because in the first

critical minutes, Bufferin speeds twice as much . . . active . . . pain reliever . . . to your headache as simple aspirin . . . so Bufferin goes to work in half the time. Half the time . . . that's Bufferin time." CX 29. (b) "ANNCR: What happens inside your system to plain aspirin and Bufferin? This illustrates two reasons why Bufferin is better. Most of Bufferin . . . with its extra speed . . . is already going to your headache . . . at the time most of plain aspirin . . . is still in your stomach. So with Bufferin when there's less to upset your stomach . . . there's also more pain reliever on its way to your headache. Two reasons Bufferin is better than plain aspirin for you." CX 69. (c) "ANNCR: In the first important 30 minutes Bufferin delivers twice as much pure pain reliever as the best known aspirin. Twice as much . . ." "Bufferin doesn't upset my stomach, the way plain aspirin sometimes did . . ." (CX 3). Furthermore, in many of the Bufferin advertisements, the "other than aspirin" representation is made visually by presenting an enlarged picture of the label on the Bufferin bottle which says "Twice as fast as aspirin" and the brand name, which fill the television screen (CX 44A; Ross, Tr. 7001).

260. By consistently failing to say that Bufferin's analgesic ingredient is aspirin, many Bufferin advertisements succeed in positioning the product as something quite distinct from aspirin. Consumers, therefore, would reasonably understand the Bufferin/"plain" aspirin distinction as one based on actual ingredient differences beyond the buffered/nonbuffered distinction (Ross, Tr. 8237-38). The fact that the advertisements frequently refer to aspirin as "plain" or "simple" does not change the fact that many consumers understand the distinction as one between aspirin and a pain reliever in Bufferin that is not aspirin (Ross, Tr. 8238). Thus, consumers would have understood a claim comparing aspirin and Bufferin with respect to speed and gentleness as one impliedly representing that the analgesic ingredient in Bufferin is other than ordinary (plain or simple) aspirin.

261. It is not surprising that several copy tests in evidence confirms that conclusion. For example, the following comments from copy tests on three Bufferin advertisements (CX

3A, 53A, 69A) show a state of mind reflecting the fact that consumers think Bufferin does not contain aspirin: "Relieves headache faster than plain aspirin — contains no aspirin," (CX 300K, respondent 26); "It has the better pain relieving qualities than aspirin," (CX 299I, respondent 20).

g. *Complaint Paragraph 14(A)*

262. Bristol-Myers has represented that scientific tests or studies prove that Bufferin is twice as fast as aspirin in the following advertisements: CX 2-4, 7, 10, 13, 34, 61-64, 67, 91-96, 98-100, 113-114, 721.

263. That the representations were made is shown by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7022; CX 815, CX 816).

264. In certain of the challenged advertisements explicit reference is made to underlying scientific proof: "Test publishes [sic] in medical journals show that in the first critical minutes Bufferin delivers twice as much pain reliever as simple aspirin . . ." (CX 63). Other advertisements referring to laboratory or clinical test results and graphs also made the representation by suggesting that the tests represent underlying scientific proof: "Bufferin laboratory tests show most of its pain reliever gets into the bloodstream 10 minutes sooner than plain aspirin" [Super: TEN MINUTES SOONER THAN ASPIRIN] (CX 91). See also CX 34, 92-96, 98-100.

2. *Establishment Representations*

265. The explicit references to scientific tests also imply a claim that it has been scientifically proven or established that Bufferin is faster and gentler than aspirin. Thus, all advertisements which made the claim challenged in Paragraph 14(A) (see F. 262, *supra*) also made the establishment claim challenged in Paragraphs 7(A)(1) and (2).

266. Consumers believe that when any comparative performance claim is made for a drug or medicine, there must exist a basis in scientific fact or medical opinion for such claims and that, otherwise, they would be prohibited (Ross, Tr. 7024, 7036). Indeed, as a matter of market fairness, consumers have

a right to expect, and do expect, that the advertiser has such scientific proof. Therefore, every Bufferin advertisement which contains a claim of comparative superiority over other drugs implies that such superiority has been established.

a. *Complaint Paragraphs 7(A)(1)-(5)*

267. Bristol-Myers as a matter of fact has explicitly represented that it has been established that: (a) Bufferin relieves pain faster than aspirin relieves pain (Complaint 7(A)(1)), (b) Bufferin relieves pain twice as fast as aspirin relieves pain (Complaint 7(A)(2)); (c) A recommended dose of Bufferin will not upset a person's stomach (Complaint ¶ 7(A) (4)); (d) Bufferin will upset a person's stomach less frequently than aspirin (Complaint ¶ 7(A)(5)).

268. These representations were made in the following Bufferin advertisements: (a) CX 2-4, 7, 8, 10, 13, 34A, 39A, 61A-88A, 91-96, 98, 101, 102, 109, 110, 719, 720, 721, 749-51, 761S, T, V, W, Z018-020 made the representations alleged in Paragraph 7(A)(1); (b) CX 2-4, 7, 10, 13, 34, 39, 61-64, 67A and 96 made the representations alleged in Paragraph 7(A)(2); (c) CX 61-64 made the representations alleged in Paragraph 7(A)(4); (d) CX 61-64, and 109 made the representations alleged in Paragraph 7(A)(5). However, none of the Bufferin advertisements in evidence made, either directly or by implication, the claim that Bufferin will relieve twice as much pain as aspirin as alleged in Paragraph 7(A)(3).

269. The fact that Bufferin advertisements made these representations is demonstrated by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7007-7020, 7041-55; CX 815, 816).

270. These representations were made through a variety of express statements and graphic representations conveying the claim that Bufferin's greater speed and gentleness was based on scientific or medical fact or opinion (Ross, Tr. 7007-08, 7010-11, 7013-14): (a) The representation that it is established that Bufferin relieves pain faster than aspirin was conveyed by explicit references to tests (F. 268, *supra*) and through use of the following visual techniques: computer typewriter reports

which suggest that a scientific test is being reported to consumers as if a meter were ticking out the results of tests, see, *e.g.*, CX 2, 4, 7 (Ross, Tr. 7009-10); anatomical models which suggest a medical demonstration, see *e.g.*, CX 68, 69 (Ross, Tr. 7014); clocks which consumers might expect would be used in laboratory test procedures, see, *e.g.*, CX 34, 39 (Ross, Tr. 7013); bar graphs which appear to come out of a medical report or scientific presentation reflecting data gathered as substantiation for the claim, see, *e.g.*, CX 93 (Ross, Tr. 7010), (b) The representation that it has been established that Bufferin relieves pain twice as fast as aspirin was made through explicit references to tests (F. 268, *supra*) and through the use of the clock graphic, the computer typewriter report, and anatomical models, (c) The establishment claims of gentleness and comparative gentleness were made by explicit reference to scientific tests. For example, CX 64 makes a comparative gentleness claim in such a context: "Try Bufferin. Doctors recommend Bufferin for minor pain more than any of the leading brands of aspirin. Scientific tests show that in the first critical minutes Bufferin gives you twice as much pain reliever as simple aspirin. Bufferin relieves arthritis minor pain and stiffness for hours . . . And Bufferin can prevent the stomach upset aspirin often causes . . ." In this instance, the initial references to doctors' recommendations and scientific tests provide a medical/scientific basis for the subsequent claim made, *i.e.*, that Bufferin will not upset a person's stomach (Ross, Tr. 7019). Moreover, respondent in CX 109 explicitly represented that "It has been clinically observed that Bufferin was gentler to the stomach than plain aspirin" (Ross, TR. 7022).

3. *Ingredient Disclosure (Complaint ¶ 19)*

271. A review of the Bufferin advertisements in evidence clearly shows that respondents at no time disclosed directly or by implication that Bufferin contains aspirin.

C. The Excedrin Advertisements In Evidence Made The Challenged Representations

1. *Representations of Superiority and Established Superiority (Complaint ¶¶ 7(B), 9(B))*

272. Bristol-Myers has admitted that it represented Excedrin is a more effective pain reliever than aspirin tablets (Paragraph 7, Answer of Bristol-Myers Company). The explicit claim that Excedrin is more effective for the relief of pain than aspirin is found in numerous advertisements in evidence. They include: CX 115, 116, 153-61, 164-67, 170, 171, 173, 175-77, 179-182, 184, 185, 188-191, 193, 202-207, 208, 210, 211, 724, 725, 727-36, 760Z017, 760Z020, 760Z021, 760Z023, 760Z024, 760Z025, 761Z015, 761Z016, 761Z017.

273. Typical of the language employed in making this representation are the following:

(a) "Tablet for tablet, Excedrin is 50% stronger than aspirin for relief of headache pain." (CX 115, 116).

(b) "This is David Janssen. A major hospital study indicated there is something even more effective than aspirin for pain relief. Doctors attending a medical convention held right here in Atlantic City heard these results of this study: it would take more than twice as many aspirin tablets to give the same pain relief as two Excedrin. More than twice as many aspirin to be as effective as Excedrin. Not three aspirin. Not even four aspirin. But more than double the recommended dosage of aspirin to give the same pain relief as two Excedrin. Yes, there is something even more effective than aspirin. That's the evidence doctors heard in Atlantic City. And that's what you should think about before you buy aspirin again . . ." (CX 158)

(c) ACTRESS: "What do you take for pain? If you take common aspirin tablets, there's something you ought to know: I think my pain reliever works better than your pain reliever . . ." (CX 181).

(d) MAN: "I don't practice medicine. So if I said Excedrin worked better than regular aspirin, you might not believe it. But what if there were medical evidence? Well, there is . . ." (CX 189).

(e) "ASPIRIN ISN'T BEST ANYMORE. That's the important new evidence about pain relievers . . ." (CX 204).

(f) ". . . 2 Excedrin = 3 Ordinary Tablets . . ." (CX 729).

a. *Complaint Paragraph 9(B)(2)*

274. Bristol-Myers has represented that a recommended dose of Excedrin relieves twice as much pain as a recommended dose of aspirin (Comp. ¶ 9(B)(2)). This representation was made in the following advertisements: CX 153-161, 164-167, 170, 173, 176, 182, 184, 185, 202-204, 208, 736.

275. The fact that Excedrin advertisements made this representation is demonstrated by the advertisements themselves, and confirmed by expert testimony (Ross, Tr. 7074-79) and several ASI Audience Reaction tests (CX 254, 255 and 257).

276. This representation was made through a variety of express and implied statements of Excedrin's ability to relieve twice as much pain as aspirin (Ross, Tr. 7075). Each of the challenged advertisements cited in F. 274 represents that at least twice as many aspirin tablets are needed to equal the pain relief provided by Excedrin. CX 153 is typical of language and approach of these advertisements:

(a) "DAVID JANSSEN: A major hospital study has indicated that there is something even more effective than aspirin for pain relief. Doctors here in Atlantic City heard these results of this study: it would take more than twice as many aspirin tablets to give the same pain relief as two Excedrin. Not three aspirin,

> not even four. But more than double the recommended dosage to give the same pain relief as two Excedrin. Think about that before you buy aspirin again. Excedrin . . . more effective than twice as many aspirin.''

277. These advertisements made the representation alleged in Paragraph 9(B)(2) because consumers would understand the claim that at least twice as many aspirin were needed to equal the pain relief provided by Excedrin as representing that a recommended dose of Excedrin relieves twice as much pain as a recommended dose of aspirin (Ross, Tr. 7074-79). This perception by consumers is evidenced in the focus group comments reported in ASI Audience Reaction tests of certain of these advertisements, where participants repeatedly played back the idea that Excedrin is twice as effective, or twice as strong, *i.e.*, relieves twice as much pain, as aspirin (*e.g.*, CX 254Z013; CX 255Z005, Z007; CX 257Z045; CX 258Z018).

b. *Complaint Paragraph 9(B)(5)*

278. Respondents have represented that Excedrin reduces fever more effectively than aspirin (Comp. ¶ 9(B)(5)). This representation was made in the following advertisements: CX 162, 163, 186.

279. The fact that Excedrin advertisements made the alleged representation is demonstrated by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7092-96), and CX 256, the report of an ASI Audience Reaction Test (Ross, Tr. 7094; CX 256Q).

280. This representation was made through the statement in each of the advertisements listed in F. 278, *supra*, that Excedrin has ''more pain relievers, *more fever reducers*, more total strength than the common aspirin tablet'' (emphasis added). Consumers would reasonably conclude that an analgesic product that had *more fever reducers* than aspirin would reduce fever more effectively than aspirin (Ross, Tr. 7092, 7096).

c. *Complaint Paragraphs 14(B), 7(B)(2) and 7(B)(5)*

281. Bristol-Myers has represented that the results of scientific tests or studies prove claims that Excedrin is twice as strong as and more effective than aspirin in relieving pain (Comp. ¶ 14(B)). Largely through this representation, respondents have implied that it has been scientifically proven or established that a recommended dose of Excedrin relieves twice as much pain as a recommended dose of aspirin (Complaint 7(B)(2)). Both of these representations were made in the following advertisements: CX 153-161, 164-167, 170, 171, 173, 176, 182, 184, 185, 202-204, 208, 736.

282. The fact that Excedrin advertisements made the alleged representations is demonstrated by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7086-92; 7126-28) and two reports of ASI Audience Reaction tests: CX 254 and 255.

283. These representations were made through a variety of express and implied statements of proof based on the results of medical or scientific studies for Excedrin's claim of greater strength and effectiveness than aspirin.

284. Challenged advertisements such as those cited in F. 281, *supra*, made the alleged representation by referring to medical studies and hospital tests as proof that at least twice as many aspirin are needed to equal the pain relief provided by Excedrin. Examples of this approach include:

(a) "This is where it all happened. [scene of large skyscraper] At a medical convention right here in Atlantic City. Here doctors heard new clinical evidence that there is a difference in how pain relievers perform. The results of this major hospital study: It took more than twice as many aspirin tablets to give the same pain relief as Excedrin. More than twice as many aspirin to be as effective as Excedrin. How much aspirin a pain reliever contains is one thing. How effectively that pain reliever performs is something else. And that's the important new evidence about pain relievers today. Two Excedrin . . . more effective for the relief of pain than twice as

many aspirin. Isn't it time you tried Excedrin?'' [SFX: Excedrin bottle and the words: ''More effective than twice as many aspirin''] (CX 155; see also similar language in CX 156-161).

(b) ''There's evidence that Excedrin is more effective than aspirin. Now you've been hearing that for over a year. But remember: the evidence is from a major hospital study . . . a study among patients with a kind of pain other than headache that medical science uses to compare pain relievers. In that study it took more than twice as many aspirin tablets to equal the pain relief of Excedrin. With that kind of medical evidence — isn't it time you tried Excedrin?'' (CX 173; see also similar language in CX 165).

(c) ''A hospital study early in the 1960's could find no significant difference in pain relief between common aspirin and Excedrin. But medical research did not stop there. And a more recent hospital study revealed a significant advantage for today's Excedrin . . . evidence that Excedrin is more effective than aspirin. Both studies were conducted among patients with a kind of pain other than headache used by medical science for comparing pain relievers. But in this latest study, it took more than twice as many aspirin tablets to equal the pain relief of Excedrin. Yes, more than twice as many! Since research in a hospital found evidence that Excedrin is more effective than aspirin, isn't it time you tried it at home?'' [SFX: Excedrin bottle and the words: ''Isn't it time you tried Excedrin?''] (CX 176).

As seen in example (a) *supra*, the advertisements, which all feature actor David Janssen as a spokesperson, often refer to a backdrop of a purported medical convention site (see CX 155-161).

285. The reference in the advertisements to ''a hospital study, would be understood by consumers to be a reference to

results of scientific tests or studies (Ross, Tr. 7127) as would references to "medical evidence," and "clinical evidence." The representation that at least twice as many aspirin are needed to equal the pain relief provided by Excedrin would be understood by consumers as a claim that Excedrin relieves twice as much pain as aspirin, and is twice as strong as and more effective than aspirin (Ross, Tr. 7088). Therefore, the reference to "a hospital study," and "medical evidence," as proof that twice as many aspirin tablets are needed to equal the pain relief provided by Excedrin would be understood by consumers as a representation that scientific tests or studies prove the claim (Ross, Tr. 7088-89). Therefore, the representation alleged in Paragraph 14(b) was made.

286. References to proof through scientific tests or studies is understood by consumers as a claim that it has been scientifically established that Excedrin relieves twice as much pain as a recommended dose of aspirin, since the claim would be interpreted as a statement of medical fact (Ross, Tr. 7217). Therefore, the representation alleged in Paragraph 7(B)(2) was made.

287. Confirmatory evidence that the representations challenged in Paragraphs 14(B) and 7(B)(2) were made is found in CX 254 and 255, reports of ASI Audience Reaction tests. As to the proof through scientific tests or studies, a respondent in CX 254 noted, "I think [David Janssen] said it was clinically tested" (CX 254Z014). A respondent in CX 255 thought "the commercial [CX 153] says they have proof it is four times as effective as aspirin" (CX 255Z008).

288. Advertisements making the claim that Excedrin reduces fever more effectively than aspirin (F. 278, *supra*) do not explicitly represent that this claim has been established (Complaint ¶ 7(B)(5)). However, since these advertisements make a claim of comparative superiority over other drugs, they, by their nature, imply a claim that such superiority has been scientifically established.

2. *Representations Of Superiority Over All Other OTC Internal Analgesics*

a. *Complaint Paragraph 9(B)(1)*

289. Bristol-Myers has represented that a recommended dose of Excedrin relieves more pain than a recommended dose of aspirin or any other nonprescription internal analgesic (Complaint 9(B)(1)). This representation was made in the following Excedrin advertisements: CX 115, 116, 122-128, 130-139, 141-142, 144-153, 155-157, 162, 163, 168, 169, 172, 174, 181, 183, 186, 188-191, 193, 202-211, 724, 725, 727-733, 735-741, 760Z017, 760Z021, 760Z023-25, 761Z015-17.

290. The fact that Excedrin advertisements made the alleged representation is demonstrated by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7066). Confirmatory evidence is contained in CX 310, the 1969 Excedrin Study.

291. The advertisements cited in F.289, *supra*, made the representation alleged in Paragraph 9(B)(1) because each contained the claim that it was *stronger* than any other nonprescription internal analgesic. Consumers would understand that an analgesic which was stronger than any other would relieve more pain than any other (Ross, Tr. 7066; CX 819). CX 310, the 1969 Excedrin Study, confirms that consumers would so interpret this claim: when asked to choose from among five descriptions of "extra-strength," over half the analgesics users queried ranked "more effective for severe pain" as their first or second choice (CX 310Z117).

292. Since consumers view relief of more pain as an attribute of a more effective pain reliever, consumers would understand the representation that Excedrin is a more effective Pain reliever than aspirin or any other nonprescription internal analgesic as claiming also that Excedrin relieved *more* pain than any other nonprescription internal analgesic (Ross, Tr. 7058-59; CX 819; CX 310Z115). Therefore, wherever the representation that Excedrin is a more effective pain reliever was made, the representation that Excedrin would relieve more pain than aspirin or any other nonprescription analgesic was

also made. Furthermore, since the representation that Excedrin is a more effective pain reliever than aspirin or any other non-prescription analgesic because it contains four ingredients (Complaint ¶ 9(B)(7); F. 315, *infra*) is but a variation of the representation in Paragraph 9(B)(6): it too would convey the representation that Excedrin relieves more pain than aspirin or any other nonprescription analgesic (Ross, Tr. 7086; CX 819). Thus, wherever the representations alleged in Paragraphs 9(B)(6) and (7) were made, the representation alleged in Paragraph 9(B)(1) was also made.

b. *Complaint Paragraph 9(B)(3)*

293. Bristol-Myers has represented that Excedrin relieves pain for a longer period of time than a recommended dose of aspirin or any other nonprescription internal analgesic (Complaint ¶ 9(B)(3)). This representation was contained in the following advertisements: CX 115, 116, 122-128, 130-139, 141-142, 144-153, 155-157, 162, 163, 168, 169, 172, 174, 181, 183, 186, 188-191, 193, 202-211, 724, 725, 727-733, 735-741, 760Z017, 760Z020, 760Z021, 760Z023-25, 761Z015-17.

294. The fact that Excedrin advertisements made the alleged representation is demonstrated by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7066-67, 7058-59), and by CX 310, the 1969 Excedrin Study, and CX 289 and 290, reports of copy tests conducted by the Ostberg organization.

295. This representation was made through a variety of express and implied statements of the longer-lasting relief given by Excedrin compared to aspirin and various other non-prescription internal analgesic products.

296. In many of the cited advertisements Excedrin is represented as a more effective pain reliever than aspirin or any other nonprescription internal analgesic because it contains four active ingredients. One of the active ingredients represented in these advertisements as making Excedrin a more effective pain reliever is an ingredient represented as providing "long-lasting relief." For example:

> . . . For the headache that really bothers you, take new Excedrin, the extra-strength pain reliever. Look: [different chemical formulae are sequentially depicted] this is the formula for aspirin. The heavily advertised product that talks of a new stronger formula merely adds caffeine to plain aspirin. But Excedrin has the strength of four medically tested ingredients. You get quick relief . . . *long-lasting relief* . . . a tension reliever to relax you . . . an antidepressant to restore your spirits . . . (CX 115; for similar language see advertisements listed in F. 315, *infra*).

These advertisements made the representations alleged in Paragraph 9(B)(3) because consumers would understand them as claiming that, by virtue of an added ingredient, Excedrin provided longer lasting relief than aspirin or any other nonprescription internal analgesic.

297. Many of the cited advertisements represent Excedrin as *stronger* for the relief of pain than aspirin or any other nonprescription internal analgesic (F. 289, *supra*). These advertisements made the representations alleged in Paragraph 9(B)(3) because consumers would view the ability to relieve pain for a longer period of time as an attribute of an analgesic product represented as stronger than others (Ross, Tr. 7066; CX 819, CX 310Z114, Z117).

298. The verbatim comments in CX 289 and 290, copy tests conducted by the Ostberg organization on advertisements (CX 141 and 125, respectively) containing both the "active ingredient" and "strength" claims, confirm that this representation was made. Respondents' comments regarding Excedrin included: "better, stronger and longer lasting" (CX 289Y); "works faster and gives longer lasting relief" (CX 289Z001); "it just lasted longer than other pain relievers" (CX 289Z002); "faster relief and relief lasts longer" (CX 289Z006); "Excedrin would work faster and last longer and was stronger than aspirin" (CX 289Z017); "it lasts for a longer time" (CX 290Z017).

299. Since consumers view longer duration as an attribute of superior analgesic effectiveness, consumers would also understand the representation that Excedrin is a more effective pain reliever than aspirin or any other nonprescription internal analgesic as claiming that Excedrin relieved pain for a longer period of time than aspirin or any other nonprescription analgesic (Ross, Tr. 7058-59; CX 819). Therefore, wherever an advertisement represented that Excedrin is a more effective pain reliever than aspirin or any other nonprescription internal analgesic (Complaint ¶ 9(B)(6); F. 308, *infra*) and/or that Excedrin is a more effective pain reliever because it contains four active ingredients (Complaint ¶ 9(B)(7); F. 315, *infra*) the representation that Excedrin relieves pain for a longer period of time than aspirin or any other nonprescription internal analgesic was also made (Ross, Tr. 7058-59).

c. *Complaint Paragraph 9(B)(4)*

300. Respondents have represented that Excedrin relieves pain faster than aspirin or any other nonprescription internal analgesic (Complaint ¶ 9(B)(4)). This representation was made in the following advertisements: 115, 116, 122-128, 130-139, 141-142, 144-153, 155-157, 162, 163, 168, 169, 172, 174, 181, 183, 186, 188-191, 193, 202-211, 724, 725, 727-733, 735-741, 760Z017, 760Z020, 760Z021, 760Z023-25, 761Z015-17.

301. The fact that Excedrin advertisements made the alleged representation is demonstrated by the advertisements themselves and by expert testimony (Ross, Tr. 7058-59). Confirmatory evidence is found in CX 310, the 1969 Excedrin Study; CX 255, report of an ASI Audience Reaction test; and CX 287, 288, 289 and 290, reports of tests conducted by the Ostberg organization.

302. This representation was made through a variety of express and implied statements comparing Excedrin's speed in relieving pain to the speed of aspirin and other nonprescription internal analgesics.

303. In certain advertisements consumers are represented as experiencing pain relief in a matter of minutes with Excedrin and faster than they ever had before. For example:

(a) "Over 19 million people have changed to new Excedrin for the relief of pain. Here's one of them . . . ACKERLY: I get terrible headaches from pressure and heat, and the fellow on the job said, 'Gee, I got something that'll take your headache away.' He gave me two pills and in about ten minutes my headache just left me and I said, 'Boy, what's the name of that stuff?' He says, 'Oh, it's Excedrin'" (CX 115).

(b) "ANNCR: What is an Excedrin headache? Listen . . . TESTIMONY: I was at a recording session [. . .] and I walked in there with a headache and I took two Excedrin during one of the breaks, ten minute breaks, and it was gone. The sound was still loud but it went away. ANNCR: Excedrin works fast. It has a special ingredient for quick relief. TESTIMONY: Something that works ZAP! It's really good . . ." (CX 145).

(c) "[. . .] MAN: I'd rather take Excedrin for a headache than anything else. WOMAN 2: The faster something can work the better it is. I'm all for being rid of pain . . ." (CX 146).

Advertisements making this representation convey the clear message to consumers that Excedrin relieves pain faster than aspirin or any other nonprescription internal analgesic.

304. In many of the cited advertisements Excedrin is represented as a more effective pain reliever than aspirin or any other nonprescription internal analgesic because it contains four active ingredients (Complaint ¶ 9(B)(7); F. 315, *infra*). One of the active ingredients which is represented in these advertisements as making Excedrin a more effective pain reliever is an ingredient (sometimes referred to as a "special" ingredient, see, *e.g.*, CX 145) represented as providing "quick relief" (see advertisements listed at F. 315, *infra*). These ad-

vertisements made the challenged representation because consumers would understand them as claiming that, by virtue of an added ingredient, Excedrin provided faster relief than aspirin or any other nonprescription internal analgesic (CX 819).

305. — 306. Reserved.

307. Confirmation that the alleged representation was made is also found in copy tests of a representative selection of the challenged advertisements listed in F. 300, *supra*. CX 255, a report of an ASI Audience Reaction test on CX 153; and in CX 287, 288, 289 and 290, reports of copy tests conducted by the Ostberg organization on CX 135, 122, 141 and 125 respectively. Tabulations of the main ideas communicated in both the ASI and Ostberg tests demonstrate that the representation of Excedrin as the faster pain reliever was conveyed (CX 255Z005; CX 287M; CX 288P; CX 289O; CX 290Q). Participants in CX 289, for example, understood the advertiser ads representing that Excedrin "works faster and gives longer lasting relief" (CX 289Z001); "gets rid of your headache faster" (CX 289Z004); "is better than anything on the market," "Faster relief and relief lasts longer," "a faster and better pain reliever than others on the market" (CX 289Z006); "relieves pain faster and is better than other ones" (CX 289Z009); "it works faster" (CX 289Z010, Z014); "of course, [is] better and works faster than any other" (CX 289Z011).

d. *Complaint Paragraph 9(B)(6)*

308. Bristol-Myers has represented that Excedrin is a more effective pain reliever than aspirin or any other non-prescription internal analgesic (Complaint ¶ 9(B)(6)). This representation was made in the following advertisements: CX 115, 116, 122-128, 130-139, 141-142, 144-153, 155-157, 162, 163, 168, 169, 172, 174, 181, 183, 186, 188-191, 202-211, 724, 725, 727-733, 735-741, 760Z017, 760Z020, 760Z021, 760Z023-25, 761Z015-17.

309. The fact that Excedrin advertisements made the alleged representation is demonstrated by the advertisements

themselves and confirmed by expert testimony (Ross, Tr. 7071-74). Confirmatory evidence is contained in CX 310, the 1969 Excedrin study; and CX 287, 288, 289, and 290, reports of tests conducted by the Ostberg organization.

310. This representation was made through a variety of express and implied statements concerning Excedrin's superiority to other pain relievers that referred to effectiveness or to particular attributes or dimensions of effectiveness, such as strength, speed and duration of relief.

311. Bristol-Myers has admitted that it represented Excedrin as a more effective pain reliever than aspirin tablets.

312. In certain of the challenged advertisements, Excedrin has also been represented as superior to aspirin and any other nonprescription internal analgesic in terms of the following attributes or dimensions of pain relief: (a) extra-strength; and (b) longer pain relief. The representation that Excedrin is superior to other analgesics as to one or more of these attributes or dimensions of analgesia would be viewed by consumers as a representation that Excedrin is a more effective pain reliever, since more pain relief and longer relief are viewed by consumers as components of greater effectiveness in a pain reliever (Ross, Tr. 7076; CX 819; CX 310 Z112-Z117).

313. Consumers would also understand the claim that Excedrin is a more effective pain reliever than aspirin or any other nonprescription internal analgesic because it contains four active ingredients (Complaint ¶ 9(B)(7)) as making the alleged representation because the former is but an extended statement of the latter (Ross, Tr. 7068; CX 819).

314. Confirmation that the alleged representation was made is found in copy tests of a representative selection of the challenged advertisements listed in F. 308, *supra*: CX 287, 288, 289, and 290, reports of copy tests conducted by the Ostberg organization on CX 135, 122, 141 and 125, respectively. Tabulation of the main ideas communicated in the Ostberg tests demonstrate that the representation of Excedrin as a more effective pain reliever was conveyed (CX 287M; CX 288P; CX 289O; CX 290Q). Respondents in the Ostberg tests understood the advertiser to be claiming Excedrin as: "better,

stronger, longer lasting'' (CX 289Y); ''the best pain reliever on the market'' (CX 289Z); ''among the different brands, the best'' (CX 289Z004); ''even though the others claim to be better for headaches'' (CX 289Z004); ''better than anything on the market'' (CX 289Z006); ''a faster and better pain reliever than others on the market'' (CX 289Z007); ''the best pain killer'' (CX 289Z008); ''better than aspirin and the other brands'' (CX 289Z009); ''relieves pain faster and is better than the other ones'' (CX 289Z009); ''of all the other pain relievers, . . . the best and fastest working'' (CX 289Z010); ''better. Works quicker. Ingredients are stronger'' (CX 289Z010); ''better and works faster than any other'' (CX 289Z011); ''a lot more effective and was also a pain reliever'' (CX 289Z013); ''a stronger pain reliever than the others'' (CX 289Z015); ''better than others for headache'' (CX 290Z007); ''relieves pain faster than anything else. Is more effective'' (CX 290Z011); ''the best product on the market. You should take it for all kinds of headaches;'' ''the best pain reliever made'' (CX 290Z016); ''much better than the others . . . stronger and more effective,'' (CX 290Z017).

e. *Complaint Paragraph 9(B)(7)*

315. Respondents have represented that Excedrin is a more effective pain reliever than aspirin or any other nonprescription internal analgesic because it contains four active ingredients (Complaint ¶ 9(B)(7)). This representation was made in the following advertisements: CX 115, 116, 120, 121, 124, 125, 132, 133, 138, 139, 141, 142, 144, 146-151, 209.

316. The fact that Excedrin advertisements made the alleged representation is demonstrated by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7081-82). Confirmatory evidence is contained in CX 289 and 290, reports of copy tests conducted by the Ostberg organization.

317. The challenged advertisements cited in F. 315, *supra*, typically link the general representation of greater effectiveness conveyed by the ''extra-strength'' claim to a claim which expressly or impliedly attributes this ''extra-strength'' to four

"medically proven ingredients," which are depicted graphically in a sequence of chemical formulas. For example:

(a) ". . . For the headache that really bothers you, take new Excedrin, the extra-strength pain reliever. Look: (formulae shown in sequence) this is the formula for aspirin. The heavily advertised product that talks of a new stronger formula merely adds caffeine to plain aspirin. But Excedrin has the strength of four medically tested ingredients. You get quick relief . . . long lasting relief . . . a tension reliever to relax you . . . an anti-depressant to restore your spirits . . . Tablet for tablet, Excedrin is 50% stronger than aspirin for relief of headache pain . . . New Excedrin, the extra-strength pain reliever." (CX 115).

(b) ". . . The modern Excedrin formula gives you quick relief (formulae shown in sequence); long lasting relief, a tension reliever to relax you, an anti-depressant to restore your spirits . . . Four ingredients, not just one or two. That's Excedrin . . . the extra-strength pain reliever." (CX 125).

Other advertisements (*e.g.*, CX 147-150) simply state "Four ingredients, not just one or two . . . that's Excedrin," and others (*e.g.*, CX 118 and 121) buttress the four-ingredient claim by stating "Excedrin . . . with more quantity and more kinds of ingredients . . . than leading pain tablets!"

318. Challenged advertisements such a those cited in F. 315, *supra*, made the representation alleged in Paragraph 9(B)(7) because consumers would have understood the presence of four active ingredients as being put forward as a reason for Excedrin's superior effectiveness, particularly where the number of ingredients in Excedrin is contrasted with the representedly smaller number of ingredients in other nonprescription internal analgesics ("four ingredients, not just one or two . . ."; "more kinds of ingredients than leading pain tablets") (Ross, Tr. 7081-82).

319. Confirmation that consumers so view the advertise-

ments is contained in CX 289 and 290, reports of copy tests conducted by ths Ostberg organization on advertisements (CX 141 and 125, respectively). These advertisements contained the four ingredient-chemical formula sequence. Tabulations of ideas communicated in both these tests demonstrate that the message of superior efficacy because of the presence of "more" ingredients was conveyed (CX 289O; CX 290Q), as do the verbatim comments of respondents: "there was more pain relief in Excedrin because it has four pain relief ingredients" (CX 289Z005); "Excedrin was better than most other pain relievers because it has four ingredients (CX 290Z002); "Excedrin is better and works faster than other products because of more things in it" (CX 290Z018).

3. *Representations of Established Superiority for Excedrin Over All Other Nonprescription Internal Analgesics*

320. Each of the Excedrin advertisements containing a claim of comparative superiority to any other nonprescription pain reliever implies that such superiority has been scientifically established. See F. 266, *supra*.

a. *Complaint Paragraphs 7(b)(1), and 7(B)(3)-7(B)(7)*

321. Respondents have also explicitly represented, as a matter of fact, that it has been established that:

(a) a recommended dose of Excedrin relieves more pain than a recommended dose of aspirin or any other nonprescription internal analgesic (Complaint ¶ 7(B)(1));

(b) Excedrin relieves pain for a longer period of time than a recommended dose of aspirin or any other nonprescription internal analgesic (Complaint ¶ 7(B)(3));

(c) Excedrin relieves pain faster than aspirin or any other nonprescription internal analgesic (Complaint ¶ 7(B)(4));

(d) Excedrin is a more effective pain reliever than aspirin or any other nonprescription internal analgesic (Complaint ¶ 7(B)(6)); and

(e) Excedrin is a more effective pain reliever than aspirin or any other nonprescription analgesic because it contains four active ingredients (Complaint ¶ 7(B)(7)).

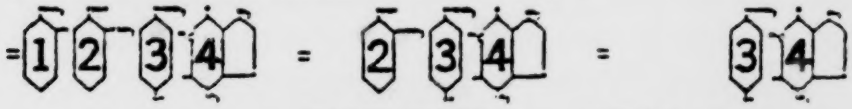
Each of these explicit representations of establishment as a matter of fact were made in the following advertisements: CX 115, 116, 124, 125, 132, 133, 138, 139, 141, 142, 144.

322. Respondent has represented that scientific tests or evidence prove that Excedrin is a more effective pain reliever than aspirin (CX 153-161, 164-167, 170-171, 173, 175-177, 179-182, 184-185, 188-191, 193, 195, 202-208, 210, 211, 760Z003-Z004, 760Z017-Z028, 761Z-Z002, 761Z015-Z017).

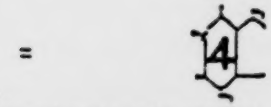
323. The fact that Excedrin advertisements made the alleged representations is demonstrated by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7117-20).

324. These representations were made through a number of express and implied statements, particularly graphic or other visual aids, of a basis in scientific or medical fact for Excedrin's superiority (Ross, Tr. 7008).

325. These advertisements feature an impressive, graphic as well as a verbal representation of Excedrin's purported four ingredient chemical formula. For example:



QUICK RELIEF LONG LASTING



TENSION RELIEVER ANTI-DEPRESSANT

Consumers would have understood these advertisements as representing that Excedrin's superiority is scientifically established. The audio-visual presentation of a chemical formula as the basis for Excedrin's superior performance would be interpreted by consumers as a statement of medical fact. The chemical formula suggests that Excedrin's difference from other nonprescription internal analgesics, and thus its superi-

ority, is due to a scientifically determined chemical structure and is a scientifically verified proposition (Ross, Tr. 7119, 7120).

326. Certain advartisements further enhance the audio-visual presentation of the formula by referring to "four medically endorsed ingredients," (CX 115, 116).

327. The audio-visual presentation of the formula consisting of four chemical components clearly suggests that the proposition that Excedrin is a more effective pain reliever than aspirin or any other nonprescription pain reliever because it contains four active ingredients (Complaint ¶ 7(B)(7)) is scientifically established. This claim subsumes the representation that Excedrin is a more effective pain reliever than aspirin or any other nonprescription internal analgesic (Complaint ¶ 7(B)(6); F. 328, *supra*). Furthermore, the representation that it has been established that Excedrin is a more effective pain reliever (¶ 7(B)(6)) would also be understood by consumers as a representation that it has been equally established that Excedrin relieves more pain and relieves pain for a longer period of time, because consumers associate these attributes of superior performance with a claim of superior efficacy (Ross, Tr. 7119). Moreover, the claims that Excedrin's greater speed and duration of pain relief are established are made even more vivid by explicit identification of those particular components in the chemical formula which give "quick relief" and "long lasting" relief. Therefore, the representations alleged in Paragraphs 7(B)(1), 7(B)(3), 7(B)(4), 7(B)(6) and 7(B)(7) are closely interconnected and have been made.

4. *Representations That Excedrin Relieves Tension, That Its Ingredients Are Other Than Aspirin Or Caffeine, And Failure To Disclose These Ingredients*

a. *Complaint Paragraph 12(B)*

328. Respondents have represented that Excedrin relieves nervous tension, anxiety and irritability and will enable persons to cope with the ordinary stresses of everyday life (Complaint ¶ 12(B)). This representation was made in the following

advertisements: CX 115, 116, 121, 124, 125, 127, 128, 132, 133, 135-139, 141-144, 148, 150, 183.

329. The fact that Excedrin advertisements made the alleged representation is demonstrated by the advertisements themselves, and confirmed by expert testimony (Ross, Tr. 7097-7101, 8246-50). Confirmatory evidence is contained in the reports of the following tests conducted by the Ostberg organization: CX 286, 287, 288, 289, 290.

330. This representation was made through a variety of express and implied statements of Excedrin's ability to perform a mood altering function apart from its ability to relieve headache or other pain (Ross, Tr. 7097-98).

331. Many of the cited advertisements state that Excedrin contains "a tension reliever to relax you and an antidepressant to restore your spirits," while chemical formulae labelled "TENSION RELIEVER" and "ANTIDEPRESSANT" are depicted graphically (CX 115, 116, 124, 125, 132, 133, 138, 139, 141, 142, 144). CX 183 speaks of "specifically, a tension reliever, a speed ingredient, an anti-depressant to put you on solid ground again."

332. In certain advertisements, situational tension is depicted or discussed and Excedrin is recommended for relief. For example:

(a) In CX 148 a consumer, after relating that he has been having money problems, claims that "when you take two Excedrin you're able to cope with your problems a lot better."

(b) In CX 135 a "woman's problem" is referred to, and Excedrin is claimed to offer "more for this time than plain aspirin. It's a combination of pain relievers and anti-depressant and . . . you can use some anti-depressing . . ."

(c) Many of the challenged advertisements depict situations which are labelled "Excedrin Headaches," and refer either to Excedrin's "tension reliever to relax you and anti-depressant to restore your spirits" (CX 124, 125, 127, 138, 139, 142, 144; F.

328, *supra*) or state that Excedrin is "made stronger against pain and its tension" (CX 128, 136, 137). In each case the advertisements depict, albeit humorously, situational tensions which are unrelated to headache or other pains. For example, in CX 133, a woman learns that her husband has wallpapered the powder room, but has glued the wallpaper upside down, and covered the medicine cabinet. In CX 136 and 137 an "Excedrin headache" is the nervous upset resulting from a rear end collision with a police car.

(d) In CX 183 a woman is shown walking on eggs and the announcer asks, "Is that how you feel when you get a headache, as though you're walking on eggs? And you feel like you'd like to smash every one of them. It's *not just the pain, it's what the pain does to you, and you want something for that too . . .*" The advertisement then refers to Excedrin's "tension reliever" and "antidepressant" to put you back on solid ground.

333. The advertisements cited in F. 328, *supra*, made the representation alleged in Paragraph 14(B) because, taking each advertisement as a whole, consumers would have understood them representing that Excedrin relieves tension and related nervous upset and restores the user to a mood where he or she can cope with the situation apart from pain relief (Ross, Tr. 7097-7101).

334. Confirmatory evidence that the alleged representation was made is found in CX 286-90, reports of copy tests conducted by the Ostberg organization on CX 183, 135, 122, 141 and 125, respectively. Each of the advertisements tested in these copy tests refers to Excedrin's "tension reliever to relax you . . . an antidepressant to restore your spirits." Tabulations of ideas communicated in each test demonstrate that the advertisements conveyed the message that Excedrin relieves tension (CX 286M; CX 287M; CX 288P; CX 289O; CX 290Q). Respondents in CX 289, for example, understood the

advertisement as representing the following claims related to tension relief: "Comparison of Excedrin to regular aspirin — pain reliever, anti-depressant, mild sedative" (CX 289Z004); "it relieves tension and it's more effective than aspirin" (CX 289Z005); "it said they are better than aspirin. They remove depression" (CX 289Z009); "if something gets on your nerves, Excedrin will help" (CX 289Z015); "they said they had something in it to combat depression and relieve the pain" (CX 289Z018); "in nerve wracking or frustrating situations, use Excedrin to calm down" (CX 290Z018).

335. A specific reference to a tension relieving ingredient in Excedrin advertisements clearly communicates to the consumer that Excedrin contains an ingredient specifically useful for tension caused by problems other than pain. This is so even where a representation of pain relief is also made (Ross, Tr. 8244-46, 8252-61).

336. Where Excedrin advertisements depict situational tensions unrelated to pain, the advertisements communicate the alleged representation despite the reference to the situations as "Excedrin headaches," the humorous treatment given the situation and the claim that Excedrin is "stronger for relief of pain and its headache" (Ross, Tr. 8266-71). The depiction of a nonpain tension situation diffuses the notion that any headache is involved, and projects an independent tension claim (Ross, Tr. 8271). CX 288, an Ostberg copy test of an advertisement of this type, confirms that these advertisements convey the representation of tension relief to consumers (CX 288P; Ross, Tr. 7105-06, 8271).

b. *Complaint Paragraph 19*

337. Excedrin advertisements do not say that Excedrin contains aspirin and caffeine (Complaint ¶ 19). None of the advertisements in evidence disclose that Excedrin contains aspirin and caffeine (all challenged advertisements for Excedrin, *i.e.*, CX 115-116, 122-139, 141-186, 188-191, 193, 202-211, 724, 725, 727-733, 735-741, 760Z017, 760Z020-21, 760Z024-25, 761Z015-17; Ross, Tr. 7113).

¶ 338. Some Excedrin advertisements speak of an ingredient which gives "long lasting relief" and another which is

an "antidepressant." While these are found on close inspection of the advertisements to be aspirin and caffeine respectively, consumers are led to believe that they are something other than aspirin and caffeine (Complaint ¶ 21; F. 337, *supra*).

339. Many of the Excedrin advertisements in evidence represent that Excedrin is a more effective pain reliever than aspirin or any other nonprescription internal analgesic because it contains four active ingredients (Complaint ¶ 9(B)(7); F. 315). These advertisements usually characterize the ingredients as giving "long lasting relief," or as acting as a "tension reliever" or "an antidepressant," but in no instance is aspirin identified as an Excedrin ingredient.

340. Some Excedrin advertisements in evidence suggest that the ingredients in Excedrin, whatever they are, do not include aspirin (CX 121, 141, 153, 159, 166, 173, 181-183, 203-204). Some advertisements claim that "tablet for tablet Excedrin is 50% stronger than aspirin for relief of headache pain" (*e.g.*, CX 115-118, 120, 121, 199). Other advertisements ask, "What's better than aspirin?" and answer, "new clinical evidence says Excedrin" (CX 203). Still others announce that "Aspirin isn't best anymore," and represent that "in a major hospital study Excedrin worked better than twice as many aspirin tablets" (CX 204) CX 183 tells consumers, "You want Excedrin. Not plain aspirin or anything in between." Such representations would be understood by consumers to mean that Excedrin is not an aspirin product (Ross, Tr. 7113, 7115).

341. Through the examples cited here and other advertisements in evidence, Excedrin has been advertised to consumers without disclosing that it contains aspirin or caffeine.

c. *Complaint Paragraph 21*

342. Respondents have also represented that the ingredient giving "long lasting relief" in Excedrin is other than ordinary aspirin and that the "antidepressant" is other than caffeine (Complaint 21). This representation was made in the following advertisements: CX 115, 116.

343. The fact that Excedrin advertisements made the alleged representation is demonstrated by the advertisements themselves, and confirmed by expert testimony (Ross, Tr. 7107-7112).

344. In fact, the ingredient identified as giving "long lasting relief" is aspirin, and the "antidepressant" is caffeine (Lanman, Tr. 121500). Yet, the advertisements contrast the ingredients in Excedrin with an aspirin/caffeine combination. The advertisements begin by telling the consumer to "take Excedrin, the extra-strength pain reliever." As the purported chemical formula for aspirin is depicted, the advertisements state, "Look: this is the formula for aspirin." Then depicting the purported chemical formula for caffeine added to aspirin, the advertisements claim that the product that "talks of a new stronger formula merely adds caffeine to aspirin." The advertisements then depict the formula for Excedrin underneath the caffeine-aspirin formula, the one bearing no apparent relationship to the other. The advertisements then state, "But Excedrin has the strength of four medically tested ingredients," and focusing on segments of the formula in turn, states, "You get quick relief, long lasting relief, a tension reliever to relax you, an antidepressant to restore your spirits" (CX 115-116).

344a. A closer inspection of the depicted aspirin-caffeine chemical formula and the Excedrin formula which is contrasted to it reveals that the formula depicted as aspirin and caffeine appears in segmented form in the depiction of the Excedrin formula. However, the aspirin-caffeine segments are arranged in such an order, and are so placed within the larger Excedrin chemical formula, that the consumer would not recognize them and would view the segments of the Excedrin formula which are stated as giving "long lasting relief" and being "an antidepressant," as something other than aspirin and caffeine respectively (Ross, Tr. 7111).

D. The Excedrin P.M. Advertisements In Evidence Made Certain Of The Challenged Representations

1. *Representations of Superiority for Excedrin P.M.*

a. *Complaint Paragraphs 9(B)(8) and 9(B)(10)*

345. Respondents have represented that a recommended dose of Excedrin P.M. will relieve more pain than a recommended dose of aspirin (Complaint ¶ 9(B)(8)) and that Excedrin P.M. is a more effective pain reliever than aspirin because it contains three analgesic ingredients (Complaint ¶ 9(B)(10)). CX 233, 235, 236, 241, 243, 244, 760Z007, 761Z007, made the representations contained in Paragraph 9(B)(8). CX 233, 241 and 244 made the representation alleged in Paragraph 9(B)(10).

346. The fact that Excedrin P.M. advertisements made the alleged representations is demonstrated by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7139-47). Further confirmatory evidence is contained in CX 263 and 264, reports of ASI Audience Reaction tests.

347. In some advertisements (CX 233 and 241), Excedrin P.M. is represented as stronger than aspirin. For example, CX 233 states that Excedrin P.M. gives you "extra-strength," a claim which consumer would understand as meaning Excedrin was stronger and more effective than aspirin (Ross, Tr. 7140). These advertisements made the representation in Paragraph 9(B)(8) because consumers would understand that an analgesic which is stronger than aspirin would relieve more pain than aspirin (Ross, Tr. 7140; see also Ross, Tr. 7066; CX 819).

348. In some advertisements Excedrin P.M. is represented as containing more pain relievers than aspirin. For example, CX 235 states that Excedrin P.M. . . . "has more pain relievers than simple aspirin" (for similar language see CX 236). These advertisements made the representation alleged in Paragraph 9(B)(8) because consumers would understand the repre-

sentation that Excedrin P.M. has more pain relievers than aspirin as claiming that Excedrin P.M. would relieve more pain than aspirin (Ross, Tr. 7140).

349. In some advertisements (CX 233, 241, 244) Excedrin P.M. is represented as containing three pain relievers. For example, CX 243 states that Excedrin P.M. "combines a mild sleeping aid with 3 pain relievers." These advertisements made the representations alleged in Paragraphs 9(B)(8) and 9(B)(10) because consumers would view the representation that Excedrin P.M. contains three pain relievers, *i.e.*, more pain relievers than aspirin, (a) as claiming that Excedrin P.M. would relieve more pain than aspirin (Complaint ¶ 9(B)(8)) (F. 345, *supra*) and (b) as a reason for Excedrin P.M. being a more effective pain reliever than aspirin (Complaint ¶ 9(B)(10)) (Ross, Tr. 7141).

350. Confirmation that these representations were made is found in CX 263 and 264, two ASI Audience Reaction tests of CX 233, an advertisement containing both the "extra-strength" and "three pain relievers" claim. Tabulations in these tests show that the advertisements conveyed the message that Excedrin P.M. was stronger, or more effective (CX 263R; CX 264Y) and contained three pain relievers (CX 263R). A respondent in CX 263 viewed the advertisement as "saying, that [Excedrin P.M.] is three times stronger than daytime aspirin," indicating not only an understanding that Excedrin is being represented as relieving more pain than aspirin, but as being more effective because of the presence of *three* analgesics (Ross, Tr. 7140, 7143).

b. *Complaint Paragraph 9(B)(9)*

351. Respondents have represented that a recommended dose of Excedrin P.M. is more effective for the relief of pain which occurs at night than a recommended dose of aspirin or any other nonprescription internal analgesic (Complaint ¶ 9(B)(9)). This representation was made in the following advertisements: CX 224, 228, 229, 233, 235, 236, 240, 243.

352. The fact that Excedrin P.M. advertisements made the alleged representations is demonstrated by the advertisements themselves and confirmed by expert testimony (Ross, Tr. 7133-38). Further confirmatory evidence is contained in the following ASI Audience Reaction tests: CX 260, 262, 263, 264.

353. This representation was made through a variety of express and implied claims of Excedrin's greater ability to relieve pain occurring at night, as distinct from pain generally, than aspirin or any other nonprescription internal analgesic.

354. In some advertisements, Excedrin is represented as the "extra-strength nighttime pain reliever" specially formulated for pain occurring at night. For example, CX 233 states that Excedrin P.M. is "The extra-strength nighttime pain reliever. Its special formula contains three pain relievers plus a mild sleeping aid." These advertisements clearly make the representation alleged in Paragraph 9(B)(9). Consumers would understand them as representing (1) particularly through the "extra-strength" claim, that Excedrin P.M. is more effective than aspirin or any other nonprescription internal analgesic (Ross, Tr. 7134); and (2) through the representation of a special formula for "nighttime" pain relief that Excedrin P.M. was more effective for pain occurring at night (Ross, Tr. 7134).

355. In some advertisements, pain occurring at night, when the consumer is going to sleep, is represented as different from pain occurring during the day. Excedrin P.M. is, in turn, represented as better for this type of pain because it is "more than simply a pain reliever." For example:

(a) "Merv Griffin: If you sometimes go to bed with aches and pains, the makers of Excedrin have a new idea for you. Excedrin P.M. . . . the nighttime pain reliever. Because aches and pains seem different at night . . . That's when you want more than simply a pain reliever. You also want something to help you get to sleep. That's what new Excedrin P.M. is made for. It combines pain relievers with a special ingredient to

help you sleep. So it relieves pain and its tension and helps you get to sleep . . ." (CX 224A).

(b) "Daytime pain and nighttime pain can be as different as day and night. Because at night, when its quiet, even a tiny pain can hurt a lot. You could take a simple pain reliever. But it doesn't have anything extra to help you sleep. Excedrin P.M. does . . ." (CX 228A).

These advertisements clearly make the alleged representation (Ross, Tr. 7135).

356. ASI Audience Reaction tests of some of these advertisements confirms that conclusion (CX 262-264; Ross, Tr. 7135-38). In CX 263 the verbatim comments demonstrate, *inter alia*, that consumers perceived Excedrin P.M. as specially formulated and thus more effective for pain occurring at night (CX 263Z022; Ross, Tr. 7136). The analysis of verbatim comments in CX 264 similarly indicates such a perception (CX 264Y; Ross, Tr. 7137). One participant in CX 264 noted that "there was a definite point that [Excedrin P.M.] was a different thing for nighttime pain than you would use during the day. It was more effective, so you would be able to sleep" (CX 262Z037). Another pointed to the product's seeming unique formulation for pain at night: "I would say that the combined ingredients make it unique, but somehow I had the feeling that it was Excedrin with one of the across-the-counter sleeping medications added, you know . . ." (CX 262Z043).

2. *Representations of Established Superiority for Excedrin P.M.*

357. Bristol-Myers has not expressly claimed that it has been "established" that:

(a) a recommended dose of Excedrin P.M. will relieve more pain than a recommended dose of aspirin (Complaint ¶ 7(B)(8));

(b) a recommended dose of Excedrin P.M. is more effective for the relief of pain which occurs during the

night than aspirin or any other nonprescription internal analgesic (Complaint ¶ 7(B)(9)); nor that

(c) Excedrin P.M. is a more effective pain reliever because it contains three analgesic ingredients (Complaint ¶ 7(B)(10)).

However, the cited Excedrin P.M. advertisements make express claims of superiority over other drugs and implies a claim that such superiority has been scientifically established (F. 266, *supra*).

3. *Representations that Excedrin P.M. Relieves Tension*

a. *Complaint Paragraph 12(B)*

358. Bristol-Myers has represented that Excedrin P.M. will relieve nervous tension, anxiety and irritability and will enable persons to cope with the ordinary stresses of everyday life (Complaint ¶ 12(B)). This representation was made in CX 216 and 219.

b. *Complaint Paragraph 23*

359. Bristol-Myers has represented that the mild sedative or sleep inducing agent contained in Excedrin P.M. is special and unique (Complaint ¶ 23). These representations were made in the following advertisements: CX 213-222, 224, 228, 229, 233, 234, 238, 239, 241-244, 760Z005, 761Z005, 760Z006, 761Z006, 760Z007, 761Z007, 760Z008, 761Z008.

360. The fact that Excedrin P.M. advertisements made the alleged representation is demonstrated by the advertisements themselvss and confirmed by expert testimony (Ross, Tr. 7155-56). The representation alleged in Paragraph 23 was made through statements relating to the special or unique contents of Excedrin P.M. making it a sedative (F. 361, *infra*).

361. Some advertisements prominently feature the label of Excedrin P.M. which contains the statements "The Nighttime Pain Reliever. Special Formulation." Advertisements also refer to Excedrin P.M.'s "special formula" or "special night-time ingredient," when representing the product as a

mild sedative. These advertisements made the representation alleged in Paragraph 23 (Ross, Tr. 7155-56).

c. *Complaint Paragraph 19*

362. A review of the Excedrin P.M. advertisements in evidence shows that none of them mentioned in any way the presence of aspirin in that product. Bristol-Myers' Excedrin P.M. ads did not disclose that Excedrin P.M. contains aspirin (Complaint ¶ 19).

363. All advertisements received in evidence were disseminated to the public. CX 800, 801 and 802 contain a listing of all advertisements offered by complaint counsel and, where available, information on the dates of dissemination and number of disseminations.

V.

The Scientific Evidence Supports The Allegations Of The Complaint

A. Evidence Necessary To Establish Absolute Or Comparative Analgesic Performance

1. *Well-Controlled Clinical Studies Are Necessary To Establish Comparative Efficacy of Analgesics*

364. In order to say any scientific or medical proposition is established, experts in the pertinent field require that the proposition be supported or proven by a type and quality of scientific evidence that reduces the chance for error to an acceptable level and is unlikely to be due to chance (Azarnoff, Tr. 9178; Moertel, Tr. 5529-31). Experts apply a set of basic methodological and analytical criteria to determine whether a body of evidence is sufficient to establish a proposition (Forrest, Tr. 8952, 8908-12, 8986; Moertel, Tr. 5533-45; Grossman, Tr. 7767-69; Azarnoff, Tr. 9178-82). Bristol-Myers itself considered and used the terms "established" and "proven" interchangeably in its statements dated November 14, 1967 and filed with the Federal Trade Commission in the

Matter of a Proposed Trade Regulation Rule for Non-Prescription Systemic Analgesic Drugs. In discussing the shortcomings of a report of a clinical analgesic study, Bristol-Myers there charged that, "The authors themselves do not claim to have proven, or to have established, the tentatively couched conclusions" (CX 908 for identification, p. 31; Lanman, Tr. 12033). Also see Bristol-Myers' Supplemental Comments, dated February 7, 1968 (CX 907 for identification, p. 14.)

365. It is generally agreed by scientists that the only type of evidence sufficient to establish the comparative efficacy of drugs is well-controlled clinical (or therapeutic) testing, using real patients with real symptoms (Azarnoff, Tr. 9179; Moertel, Tr. 5528-29; Grossman, Tr. 7767; Forrest, Tr. 8952, 8908-09; CX 514, pp. 35371, 35444).

366. The criteria for evaluating the reliability and validity of clinical studies used to establish the comparative efficacy of drugs include: (a) where analgesics are involved, an appropriate pain model (F. 368, 374-80), using subjective responsive methodology (F. 369, *infra*); (b) replication of results (F. 370, *infra*); (c) an experienced, unbiased investigator (F. 371, *infra*); (d) adequately trained personnel and appropriately instructed subjects (F. 372, *infra*); (e) a written, and sufficiently detailed protocol (F. 373, *infra*); (f) random assignment of patients to treatments (F. 384-87, *infra*); (g) double-blinding (F. 388, *infra*); (h) where pain is being measured, use of a placebo control (F. 389, *infra*); (i) use of appropriate statistical techniques determined in advance of tests (F. 390, *infra*); (j) use of a recognized level of statistical confidence (the 5% level) (F. 391, *infra*); (k) application of appropriate judgment as to the clinical significance of results (F. 392-93, *infra*); and (l) subjecting the study to peer review (F. 394, *infra*).

367. Other methods which purport to measure comparative efficacy, or other techniques which try to assess comparative efficacy without actual measurement, have not been shown to be sufficiently reliable for this purpose (F. 400-04, *infra*).

368. Experts who study the performance of analgesics in clinical pain have found several "pain models" amenable for their evaluations. Surgical pain, orthopedic pain, post-operative pain, cancer pain, post-partum pain, pain from dental extraction, and headache pain have all been used in well-controlled clinical studies that have assessed the comparative efficacy of analgesics (Forrest, Tr. 8911; Beaver, Tr. 6045; CX 514, p. 35382).

369. Since pain is a personal and subjective experience, the best way to establish the comparative efficacy of OTC analgesics is to elicit the subject's own report of the pain experienced and the degree of relief obtained after administration of the drugs under study — the subjective response methodology (Forrest, Tr. 8908-10; Moertel, Tr. 5534; CX 514, pp. 35377, 35444). There are no objective measures of pain relief in the clinical situation (Forrest, Tr. 8916).

370. In order to establish the comparative efficacy of drugs, including OTC analgesics for the relief of mild to moderate pain, at least two well-controlled, separately conducted studies on the drugs in question are required (Brown, Tr. 4878, 8160-61; Forrest, Tr. 8917; Grossman, Tr. 7769; Moertel, Tr. 5530, 5850-51; Azarnoff, Tr. 9180, 9185-86; CX 514, pp. 35371, 35445). Replication of results in the hands of separate, competent investigators reduces the likelihood that the original results were due to chance (Azarnoff, Tr. 9185; Brown, Tr. 8161; Moertel, Tr. 5850; Grossman, Tr. 7769) and avoids the possibility that errors or artifacts in the design or execution of any one study are carried over into the next (Moertel, Tr. 5851; Brown, Tr. 8161). As Dr. Brown said:

> You don't want two studies, neither of which are convincing. You want two studies that, by themselves — each study should stand by itself. Then the question is, if you can replicate a persuasive study in several laboratories, then you are really persuaded that it isn't a fluke of the laboratory or fluke of the investigator (Brown, Tr. 8161).

371. A threshold requirement for an adequate and well-controlled study is an experienced investigator (Forrest, Tr. 8921; Moertel, Tr. 5533-34). Moreover, the motivation of an investigator is a possible source of bias, and it is therefore important to ensure that the investigator is truly independent (Moertel, Tr. 5534).

372. Whereas nurses or other persons are used to administer treatments, and to observe and record the subjective responses of patients under study, it is of course important that they be adequately trained and experienced to guard against distortion of this information provided by patients (Brown, Tr. 4976-78; Forrest, Tr. 8921; Moertel, Tr. 5541-42). In out-patient clinical studies, where patients are ambulatory and record their own responses to treatment, the chance for distortion in recording responses by a nurse or other third party is virtually eliminated; but the patients themselves must be instructed to properly record their responses (Moertel, Tr. 5541; Forrest, Tr. 9123-24; Beaver, Tr. 5965; Azarnoff, Tr. 9231-33).

373. A written protocol which sets down in detail the objectives of the study and how those objectives are to be met before the study begins is essential if the study is to be well-controlled (Moertel, Tr. 5537). Such a protocol should cover not only features of study design, but also a plan for its analysis (Moertel, Tr. 5542; Azarnoff, Tr. 9180, 9183; F. 390, *infra*). Strict adherence to such a protocol provides a reader with an additional opportunity to judge whether there was an opportunity for uncontrolled bias to enter into the conduct of the study (Moertel, Tr. 5542-43).

374. The clinical study must employ a pain model that is appropriate for the conclusions sought to be drawn from it (Moertel, Tr. 5537). In general, the best pain model is the type(s) of pain for which use of the drug is intended or for which a claim of efficacy may be made (Moertel, Tr. 5535-37; Azarnoff, Tr. 9185; Forrest, Tr. 8911; Evans, Tr. 6352-53). Where a claim relates to comparative efficacy for headache pain, at least one of the well-controlled studies required to establish such claim should be in headache pain (Smith, Tr.

5442; Forrest, Tr. 8911; Moertel, Tr. 5537). The need for at least one study to focus on the type of pain for which a claim is made, *i.e.*, headaches, is especially acute where the product involved is a combination of ingredients, like Excedrin, which may act differently in different pain models (Beaver, Tr. 6048-51).

375. Bristol-Myers apparently agreed — at least as of early 1968 — with the proposition that clinical studies must focus on headache pain if they are to be used as a basis for claims concerning superiority in headache. In Supplemental Comments, dated February 7, 1968, filed before the Federal Trade Commission in the *Matter of a Proposed Trade Regulation Rule for Nonprescription Systemic Analgesic Drugs*, Bristol-Myers asserted that OTC analgesics will function differently in different kinds of headaches, and that, therefore, their performance in pain models far removed from headaches, such as post-partum and post-surgical pain, are not transferrable to ordinary headaches (Lanman, Tr. 12013-14). Bristol-Myers also quoted Dr. John Seed, an expert recognized in the field of analgesics, and a co-author with such analgesics experts as Drs. Houde, Beaver and Bellville, who stated:

> If one wants to claim that [an] analgesic relieves menstrual cramps, one has to test it on patients with menstrual cramps. If one wants to claim it relieves tension headache, one has to test it on tension headaches. If one wants to claim that it acts faster on tension headache than some other preparation, one should be required to prove that it acts faster; i.e., by interviewing people under the proper conditions and finding out how soon the headache goes away (Lanman, Tr. 12020-21).

376. Throughout its February 7, 1968 Comments, Bristol-Myers also cited the opinions of numerous recognized experts in clinical analgesia to support its position that an analgesic may be effective against one type of pain and not against another, or that the comparative efficacies of analgesics may differ depending upon the particular pain model studied

(Lanman, Tr. 12020-27). For example, Bristol-Myers cited Dr. Max Sadove, an expert who had published widely in the field of analgesics, who stated, *inter alia*:

> one merely gets a hint in any of the usually done studies of what might be expected of the drug. Even if one designs it with placebo controls and cross over design and a sufficient number of patients. *The reason is that the drug may be effective against one type of pain and not against another*. (Lanman, Tr. 12021-22, underscoring by Bristol-Myers).

Bristol-Myers also cited Dr. Louis Lasagna, who was Chairman of the NAS/NRC Panel responsible for CX 511 (F. 23, *supra*), who stated:

> If a drug is shown superior to another drug, or to a placebo, in three or four different clinical states accompanied by pain, and the results are in general agreement, then it would be a reasonable assumption to guess that these same relationships will occur in other kinds of pain that have not been studied. *This is, however, a matter of opinion and educated guessing rather than established fact*. (Lanman, Tr. 12024; underscoring by Bristol-Myers).

377. Bristol-Myers also cited Dr. Walter Modell, former professor of pharmacology at Cornell and current, long-time editor of the *Journal of Clinical Pharmacology and Therapeutics* (Lanman, Tr. 12025-26). Dr. Modell stated that the particular factors responsible for headache pain — which (1) operate within the cranium, in tissues outside but adjacent to the skull, and in certain cranial and cervical nerves and which (2) relate to vascular distension, traction and pressure, local tissue inflammation and muscular spasms — are so different from mechanisms centered in other areas of the body involving different nerve pathways that pharmacological data gathered with respect to these other areas would not be reliable with respect to analgesics' performance in headaches (Lanman, Tr. 12025).

378. Regarding Bristol-Myers' February 7, 1968 Comment to the Commission (CX 907 for identification), Dr. Lanman, Bristol-Myers Product's Medical Director for the past 17 years, testified on cross-examination that he "would have to assume responsibility" for the views stated in the documents (Tr. 12028). However, upon redirect examination Dr. Lanman testified that in fact he had not seen a copy of CX 907 or 908 until the previous day's examination when they were handed to him by complaint counsel (Tr. 12183-84). The documents (CX 907 and 908 for identification) do not bear the signature of Dr. Lanman but bear that of Gilbert H. Weil, Bristol-Myers' counsel. Dr. Lanman himself believed, at least in the 1960's, that a clinical analgesic study limited to subjects in normal post-partum pain could not be used as a basis for generalizations about the effectiveness or side effects of an analgesic (Lanman, Tr. 12027; CX 909).

379. Respondents' expert Dr. Sunshine testified that the FDA requires submission of at least two studies on new drugs that purport to be analgesics, and he stated that proposed FDA guidelines require that the second study be performed on a different kind of pain than that studied in the first because one could not be sure that the mechanism of action may be the same in another pain model (Sunshine, Tr. 9823-25). In fact, Dr. Sunshine was involved in preparing the guidelines which called for studies in different kinds of pain for new drugs (Sunshine, Tr. 9824-25).

380. Bristol-Myers' position with headache pain studies is that "subjective response clinical studies cannot be done using headache as the pain model" (RPF 964-982). However, the record as a whole does not show that superior effectiveness of Excedrin for headache pain cannot be demonstrated. It simply shows that a subjective response study of headache pain is more difficult than a similar study of some other pain, for example, post-partum pain (Tr. 6057, 6060).

381. Dr. Lanman, Bristol-Myers' Medical Director, testified that a methodology has not been developed for a satisfactory study of headache pain. Bristol-Myers has approached two recognized investigators in the headache pain study field

and they have declined to conduct headache pain studies for Bristol-Myers. However, according to Dr. Lanman, Bristol-Myers is trying to develop new methods and techniques for headache pain study (Tr. 11729-31).

382. The record shows that in a headache pain study there are more factors that must be controlled than in other pain studies. However, it is a matter of degree only and does not show that a headache pain study is not feasible (RPF 964-967, 973-76, 980-82). The FDA Analgesic Panel Report lists six reported headache studies using aspirin, one of which appeared in 1967 (CX 514, pp. 35382-83).

383. Studies of comparative analgesic efficacy for simple headache pain must necessarily be conducted in an outpatient setting (Sunshine, Tr. 9651-52). While attention must be directed towards careful control and instruction of the patients involved in outpatient studies, such research has been successfully conducted with respect to headaches, other kinds of pain (*e.g.*, oral surgery, angina pectoris) and other measures of drug performance besides pain (*e.g.*, anti-emetics) (Beaver, Tr. 5965, 6073; Forrest, Tr. 8985-86, 9140-42; Brown, Tr. 8115-17; Azarnoff, Tr. 9184-85; 9232-33; Sunshine, Tr. 9652, 9751-53). In this proceeding, Bristol-Myers itself relied on two outpatient studies on pain, one of which examined headache pain, in an attempt to support its position that caffeine adds to the analgesic effect of aspirin and acetaminophen (Lanman, Tr. 11512-17, 12066-67, 12083-84).

384. It is essential in any well-controlled study for subjects to be randomly assigned to the various treatment groups under study (Brown, Tr. 4858-60, 4911; Forrest, Tr. 8912; Azarnoff, Tr. 9179-80; Evans, Tr. 6342; Grossman, Tr. 7767-68; Moertel, Tr. 5543; Laska, Tr. 10166; CX 514, p. 35444). The randomization process is necessary to balance out those variables in the subject population and in the design and conduct of the study itself that cannot be identified and controlled directly by the investigator (Forrest, Tr. 8916; Azarnoff, Tr. 9180; Beaver, Tr. 6019-21; Sunshine, Tr. 9684). The randomization process is the prerequisite for concluding that

the uncontrolled variables inherent in all research is fairly balanced across the treatment groups (Laska, Tr. 10585-86). It is, therefore, fundamental to the validity of the study and the interpretation of its results (Forrest, Tr. 9114-15; Laska, Tr. 10585-86; Brown, Tr. 4911, 4994-95, 5008, 5083-84). Unless a particular study is properly randomized, the validity of that study is questionable and all analyses of its results are compromised (Forrest, Tr. 9114-15, 9121; Brown, Tr. 5083-84, 8038; Laska, Tr. 10270).

385. A technique to assure that important, identifiable variables are balanced fairly across treatment groups is to stratify all subjects on such variables (*e.g.*, level of initial pain) and then randomly assign subjects within each stratification to the various treatment groups (Azarnoff, Tr. 9180; Sunshine, Tr. 9725-26). Such a procedure will ensure that these critical variables will be represented fairly equally in all treatment groups (Azarnoff, Tr. 9180; Moertel, Tr. 5544; Sunshine, Tr. 9716, 9725-26).

386. A failure to randomize properly may actually be similar to not having attempted randomization in the first place (Forrest, Tr. 8921). That is, the results of inadequately randomized studies may be as attributable to factors which have unequal impact on the treatment groups as they may be to the actual performance of the treatments themselves (Forrest, Tr. 8918-21).

387. Imbalances or inequalities on study variables at the outset of a study can be an accidental result of the procedure by which subjects are assigned to treatments (Moertel, Tr. 5544; Sunshine, Tr. 9662; Laska, Tr. 10260-64). Use of randomization in that assignment procedure is supposed to guard against such baseline imbalances or inequalities and the attendant problems in interpreting results (Brown, Tr. 5083-85; Forrest, Tr. 8916; Beaver, Tr. 6022-23). In certain cases, statistical techniques may be available to readjust or "correct" for such baseline inequalities and to render results interpretable (Moertel, Tr. 5544; Laska, Tr. 10269; Brown, Tr. 5086-87; Forrest, Tr. 9121). However, the magnitude of the observed imbalance, and the importance of the variable on

which the imbalance occurs, are crucial factors in determining whether such statistical correction of baseline imbalances restores the study's validity (Brown, Tr. 4911-12, 8052-54, 8146; Forrest, Tr. 9121).

388. An inflexible prerequisite of any well-controlled clinical study, and particularly in the area of mild analgesic drugs and pain relief, is double-blinding. That is, neither the test subject nor the investigator should be able to tell which treatment is being administered (Azarnoff, Tr. 9180; Evans, Tr. 6354, 6357; Moertel, Tr. 5538; Grossman, Tr. 7767-68; Forrest, Tr. 8912; Sunshine, Tr. 9676-77; Laska, Tr. 10166; CX 514, p. 35444). Responses to analgesic drugs can be significantly affected by subjects' pre-existing biases or beliefs and expectations (Beaver, Tr. 6016; Moertel, Tr. 5538; Forrest, Tr. 9052; Evans, Tr. 6357-62; Brock, Tr. 8556-61). The whole point of the double-blind technique is to separate out the effect of expectation from the true pharmacologic effect of the drugs tested (Beaver, Tr. 6014). Moreover, the conscious or unconscious biases of the investigator, nurse observers, the subjects and others involved in the conduct of the study can exert an effect that distorts the action of the actual treatments administered (Evans, Tr. 6341, 6357-62; Moertel, Tr. 5538). Double-blinding effectively controls the expectations and beliefs of subjects and the biases and influences of those conducting the study by assuring that these extraneous effects cannot differentially impact on any particular treatment (Beaver, Tr. 6014-16; Evans, Tr. 6360). Strictly speaking, patient expectations and investigator biases can not be entirely eliminated, but double-blinding at least assures that all treatments in the study will be equally affected (Azarnoff, Tr. 9180; Beaver, Tr. 6015; Forrest, Tr. 8916; Evans, Tr. 6360). To achieve an adequately double-blinded study, it is essential that the treatments look the same, taste the same and appear the same in all respects, so that the subjects in one treatment group will not be prompted to expect something different from subjects in another and investigators will have no clue as to which treatment they are administering (Azarnoff, Tr. 9180; Beaver, Tr. 6023-24).

389. Whenever possible, a well-controlled study comparing the efficacy of two drugs, particularly mild analgesics, should include a placebo control (Forrest, Tr. 8922; Moertel, Tr. 5539-41; Azarnoff, Tr. 9181; Beaver, Tr. 5979-81; CX 514, pp. 35444-45). The placebo, a pharmacologically inert substance, acts as a separate treatment in the study, and it serves as a built-in measure of the sensitivity of the study and as an analytical tool to aid in the analysis of its results (Forrest, Tr. 8923, 9008-09; Moertel, Tr. 5539-41; Azarnoff, Tr. 9181). Unless the results of a study demonstrate its ability to distinguish a standard analgesic compound — such as aspirin — from placebo, one cannot be certain that the study was sufficiently sensitive to detect differences between the standard and test compounds under study, even if such differences in fact existed (Forrest, Tr. 8923; Moertel, Tr. 5539-41; Beaver, Tr. 5979-80; Lanman, Tr. 12092-93). Similarly, in the absence of a placebo control, the failure to find a difference between the treatments under study may be due to insensitivity in the study methodology rather than to the fact that no difference exists between the treatments (Beaver, Tr. 5979-81; Forrest, Tr. 9008).

390. The statistical techniques for analyzing the results of clinical trials should be set out in advance and should be appropriate to the design and purpose of the study (Azarnoff, Tr. 9180, 9183; Moertel, Tr. 5542). Deciding upon the statistical analysis in advance guards against the investigator peeking at the data and, perhaps, aborting a study before completion when a desired result has been reached or choosing to analyze only those segments of the study that may show favorable results (Moertel, Tr. 5542-43). Failure to adhere to statistical procedures set forth in advance introduces a bias into the analysis (Azarnoff, Tr. 9183). Such "data massaging" destroys the validity of the analysis (Moertel, Tr. 5543).

391. When studies are designed for the purpose of establishing differences between the treatments under study, there must be a method to judge whether any observed differences may be due to chance or simple random variations in the data generated rather than to actual differences in the effects of the

treatments (Brown, Tr. 4867-69; Moertel, Tr. 5545). When the observed differences are shown through appropriate statistical analyses to be significant at or beyond the 95% level, scientists will accept those differences as real and not being due to chance (Azarnoff, Tr. 9182; Brown, Tr. 5143; Forrest, Tr. 8912; Moertel, Tr. 5545-46). Scientists are not willing to accept greater than a 5%, or one in 20, likelihood that the differences observed in a study are due to chance (Azarnoff, Tr. 9182; Brown, Tr. 5143; Moertel, Tr. 5545). This maximum 5% chance likelihood as a standard for statistical significance is generally accepted in the scientific community, including the scientific literature (Brown, Tr. 5138-40, 5142-43; Moertel, Tr. 5545; Forrest, Tr. 8912; Azarnoff, Tr. 9182; Laska, Tr. 10551-53).

392. When an observed difference between two drugs is determined to be statistically significant at or beyond the 95% level, clinicians who evaluate the results of studies on analgesics also address the separate question of whether such statistically significant differences have clinical importance (Beaver, Tr. 5971-72; Moertel, Tr. 5609-13; Forrest, Tr. 8912, 8915; Azarnoff, Tr. 9182-84). As Dr. Beaver stated:

> . . . the difference, to be a difference, must make a difference. What we would normally do is say if the difference is small beyond a certain point, it may, in fact, exist but it doesn't make any difference. It does not serve as a reasonable basis for choosing one product over another [or] making a particular claim about a product. (Beaver, Tr. 5971).

393. Selection of any specific, objective standard of the clinical importance — as opposed to the statistical significance —of differences between drugs is exceedingly difficult (Laska, Tr. 10459). It is clear that unless a difference is statistically significant at or beyond the 95% level, it cannot be clinically important (Moertel, Tr. 5611; Forrest, Tr. 8912; Azarnoff, Tr. 9183-84). On the other hand, by using a large number of patients, it is possible to demonstrate the statistical significance, at the 95% level, of minute differences (Moertel,

Tr. 5610). Therefore, a meaningful way to resolve concerns over the magnitude of difference necessary for clinical importance is to require statistically significant differences to be obtained with a reasonable sample size, and no greater (Forrest, Tr. 8914). Generally, past studies comparing the efficacy of analgesics, which have provided results that clinicians have acted upon as clinically important, have had sample sizes in the area of 20-50 subjects per treatment (Forrest, Tr. 8913; Sunshine, Tr. 9772-75). With allowances provided for the additional levels of within-study variation that are inherent in studies of mild OTC analgesics, Dr. Forrest concluded that if a well-controlled study could demonstrate statistically significant differences (at the 95% level) between mild analgesic treatments with no more than 50 to 60 subjects per treatment, he would accept those results as clinically important (Forrest, Tr. 8914-15). If more subjects are required to demonstrate the statistical significance of observed differences, their clinical importance diminishes (Forrest, Tr. 8915).

394. Subjecting a clinical study to peer review, which occurs when a study is submitted for publication in a reputable journal, adds another indication of reliability and allows greater confidence in a study (Moertel, Tr. 5545; Forrest, Tr. 8921). One of the important criteria used in coming to a conclusion about the validity of a study is whether it is published and whether, thereafter, it meets with the acceptance of other scientists and, ultimately, whether the study is replicated by others (Brown, Tr. 4915).

395. The standards for well-controlled clinical trials necessary to establish a claim of absolute or comparative efficacy between drugs are and have been well accepted in the scientific community by experts in the design and analysis of such studies for years (Moertel, Tr. 5545; Forrest, Tr. 8923; Azarnoff, Tr. 9178). The FDA Panel on OTC Analgesics has incorporated these principles and requirements for well-controlled clinical studies into its Final Report (CX 514, pp. 35371, 35444-45), and FDA has codified many of these principles into its regulations mandating the need for "substantial

evidence'' to support effectiveness claims for drugs (21 C.F.R. § 314.111(a)(5)(ii)(a) through (c)).

2. *Evidence Other Than Well-Controlled Clinical Studies Is Insufficient to Establish Superior Efficacy of One OTC Oral Analgesic Product Over Another*

396. Various attempts to measure the absolute or comparative efficacy of analgesics other than by well-controlled clinical trials using appropriate pain models have not been shown sufficiently reliable to establish absolute or comparative efficacy of analgesic agents in man and are not accepted either by experts in the evaluation of analgesic agents or by the FDA (F. 397-404, *infra*).

397. Consumers' perceptions of therapeutic superiority of one product over another product are not reliable evidence for the purpose of establishing the efficacy or comparative efficacy of OTC analgesics because consumers are unable to evaluate for themselves the true pharmacologic efficacy of drugs (Moertel, Tr. 5631, 5749-59; Evans, Tr. 6354-60; Azarnoff, Tr. 9196; Grossman, Tr. 7887-89). Of course, consumers do perceive that they feel better, or that they hurt less after swallowing a pill (Grossman, Tr. 7787-89; Evans, Tr. 6354-55, 6357). The inability to ''evaluate'' in this context simply refers to consumers' inability to distinguish the true pharmacologic contribution of a drug from a host of factors that have nothing to do with the drug's true pharmacologic effect (Moertel, Tr. 5749-55; Beaver, Tr. 6020; Forrest, Tr. 9052; Evans, Tr. 6355; Azarnoff, Tr. 9196; Grossman, Tr. 7887-89).

398. A consumer's expectations of what a drug will do are an important factor and play a powerful role in influencing his response to the drug (Brock, Tr. 8556-61; Beaver, Tr. 6014, 6016; Evans, Tr. 6355-56). However, such responses do not reflect the true pharmacologic action of the drug and should not be relied on for the purpose of determining whether a drug is effective or whether one drug is more effective than another. The simple reason is that a consumer's expectations are af-

fected by many extraneous factors, such as his or her disposition, advertising, past experience with the drug, relationship with the physician or nurse administering the pill, and even the size, shape and taste of the pill taken (Evans, Tr. 6355; Moertel, Tr. 5751-52). In fact, in cases where the effect of a drug is somewhat indeterminate or where the consumer has no yardstick or information about its effect, he may well be dependent upon extraneous information or suggestion for making up his mind about what the effect of the drug is (Brock, Tr. 8556-61).

399. Thus, consumers on an unblinded basis cannot differentiate between a true pharmacologic response of a drug and a response due to extraneous factors, such as suggestions or expectations, that surround the taking of the drug. The influence of expectations or suggestions are so real that even blinded subjects in a controlled test report pain relief from a placebo (Forrest, Tr. 9050, 9052; Evans, Tr. 6326-30). This phenomenon is known as the "placebo effect" among medical-scientific investigators. The placebo effect is typically reported in the scientific literature to produce subjective pain relief in over 30% of test subjects in controlled analgesic studies (Evans, Tr. 6324, 6328-29; Laska, Tr. 10492). Anyone on any occasion can be a "placebo responder" (Laska, Tr. 10493-94). Expectations and similar factors, and hence the "placebo effect," can never be totally eliminated from any situation where a human suffers pain, but well-controlled testing methodologies can control expectations and other nonspecific factors, and therefore the placebo effect, by ensuring that the treatments under study are equally affected by them (Beaver, Tr. 6015, 6019; Evans, Tr. 6340-43; F. 384, *supra*). Balancing nonspecific factors across the treatments in a study, through techniques of randomization, blinding and the other controls already discussed (F. 384-87, *supra*) is the only accepted way that human tests can be expected to provide reliable information about the true efficacy and comparative efficacy of drugs (Beaver, Tr. 6014-25; Evans, Tr. 6340-48, 6354-63).

400. The fact that an OTC analgesic contains a combination of ingredients, or more ingredients than another OTC an-

algesic, is not acceptable evidence that it is more effective (Azarnoff, Tr. 9188; Forrest, Tr. 8977-78). In order to conclude that one analgesic--even with more ingredients--is more effective than another, one needs adequate, well-controlled clinical studies (Forrest, Tr. 8977-78).

401. For many drugs, the relationship between the blood levels and the drug's effect has been determined. However, in the case of aspirin or aspirin products, no direct correlation has yet been scientifically established between the amount of aspirin appearing in the bloodstream at any time point and the degree of onset, intensity or duration of pain relief afforded by aspirin. Therefore, "blood level" studies, *i.e.*, studies that simply examine the amount of a drug in the bloodstream at various time intervals following ingestion, are not a reliable basis for predicting comparative analgesic performance beyond that the general level of aspirin in blood (serum salicylate concentration, or blood level) associated with pain relief is known. The unique characteristics of aspirin in this regard has been attested to by qualified expert witnesses who testified in this proceeding (Azarnoff, Tr. 9189-90; Beaver, Tr. 5945-46; Forrest, Tr. 8987-90; Moertel, Tr. 5801-05, 5817-18, 5860). This view is shared by the FDA Panel on OTC Analgesics (CX 514, pp. 35359, 35361, 35374, 35377-78), by a panel of well-respected experts convened by the National Academy of Sciences/National Research Council to evaluate various claims for analgesics (CX 511F; F. 22-26, *supra*), by the *AMA Drug Evaluations* prepared by a panel of experts to evaluate evidence bearing on the performance and comparative performance of drugs (CX 512H, CX 518G; F. 216-23, *supra*); and by the *Medical Letter*, a recognized publication relied upon by physicians and other scientists for information relating to the performance of medicines (CX 510A, B; F. 225-28, *supra*).

402. Thus, clinical studies which simply show that one analgesic preparation is absorbed more rapidly into the bloodstream than another cannot lead to conclusions with respect to the comparative speed of the analgesics in relieving pain.

403. Studies employing experimental pain, *i.e.*, pain induced in humans in the laboratory by various artificial de-

vices, are not sufficiently reliable for use in establishing the comparative efficacy of OTC analgesics. Experimental pain studies have failed to predict with any consistency the clinical performance of analgesic drugs, particularly those used for OTC medication (CX 514, p. 35444; Evans, Tr. 6353; Elvers, Tr. 11087-88). Pain induced in the laboratory by various artificial means is significantly different from pathological pain or pain in natural state, and for this reason the performance of analgesic drugs in relieving pathological pain must be determined in the clinical setting (Evans, Tr. 6353; CX 425C; F. 544, *infra*).

404. While more advanced forms of experimentally induced pain, such as submaximum tourniquet pain (where the subject's arm is cuffed, and the arm worked until pain is induced), come somewhat closer to imitating pathological pain (Evans, Tr. 6338-39), even these have been found by experienced investigators to be insufficiently reliable predictors of analgesic performance (Evans, Tr. 6375; Elvers, Tr. 12352). The problem of simulating clinical pain in the laboratory is so complex that results obtained with presently employed experimental pain producers can, in fact, be seriously misleading (Elvers, Tr. 11189-90).

B. The Design of In-Patient Clinical Studies To Assess Comparative Analgesic Performance

405. Studies of analgesic performance in man rely of necessity upon the verbal reports of patients in pain to generate the data which are then analyzed (Forrest, Tr. 8869-70; F. 369, *supra*). Typically, before hospitalized patients are accepted into a clinical analgesic study, they will be interviewed by an observer/investigator to obtain their history, their consent to participate and to ascertain the level of their pain prior to treatment (Brown, Tr. 4976-78, 4981-82, 4985; *see e.g.*, CX 425Z002; Smith, Tr. 5405; CX 454C). This baseline, or initial pain level, is determined by the patient's statement that she is in "severe" pain, "moderate" pain, "slight" pain or "none" (Brown, Tr. 4988; CX 425Z002; Smith, Tr. 5404-05; CX 454C). Researchers generally seek patients in "severe" or

"moderate" initial pain so that the pain reducing properties of the compounds under study will have fairly good opportunity to perform (Forrest, Tr. 8882-83; Smith, Tr. 5431-32). Indeed, some researchers seek to confine patients to those in "severe" pain to maximize the opportunity for observing any differential performance of the test compounds (Forrest, Tr. 8882-83).

406. Pain relieving performance is typically measured in two ways: (1) reduction in pain intensity; (2) amount of pain relief (Smith, Tr. 5419; Brown, 4880-82). That is, at fixed intervals following the initial interview and the administration of a blinded treatment, patients are asked (1) to describe the amount of their pain as "severe," "moderate," "slight," or "none," and (2) to describe the amount of pain relief they have experienced as "complete," "more than half," "less than half" or "none" (Smith, Tr. 5406-08; CX 454C; Brown, Tr. 4880-82). The difference in pain intensity is quantified by first assigning numerical values to the levels of pain intensity possible. For example, "severe" is frequently given a value of 3; "moderate" a value of 2; "slight" a value of 1; and "none" a value of 0 (Brown, Tr. 4882; Smith, Tr. 5406; CX 454C; CX 425Z007).

407. The pain intensity difference (P.I.D.) between the baseline or pre-treatment pain level and the pain level at the time of the first post-treatment interview is calculated by simply subtracting the pain intensity score at this interview from the initial pain intensity score (Brown, Tr. 4881-82). Thus, if a patient started in pain which she described as "severe" and, after one-half hour (or some other fixed interval) described her pain as "slight," her pain intensity difference (P.I.D.) score would be 2 (*i.e.*, "severe" (a score of 3) minus "slight" (a score of 1) equals 2) (Brown, Tr. 4881-82). The patient's pain relief is also quantified by assigning an appropriate numerical value to the patient's statements at succeeding interviews, that their pain, for example, has been "completely relieved," "more than half relieved," "less than half relieved," or "no relief" (Smith, Tr. 5406-07; CX 454C).

408. A pain intensity difference (P.I.D.) score can be calculated for each succeeding interval (generally one hour) after

treatment by subtracting the patient's pain score for that interval from the baseline, pre-treatment pain score (Brown, Tr. 4881-82; Smith, Tr. 5404-06). A pain relief score can be determined for each interval by assigning the appropriate numerical value to the patient's level of relief reported at each succeeding interval (Brown, Tr. 4881-82; Smith, Tr. 5406-08).

409. If a study is designed to last six hours, and to include six hourly post-treatment interviews, each patient who completes the study will have six (6) P.I.D. scores and six (6) pain relief scores (Smith, Tr. 5420-21; Brown, Tr. 4881-82). The standard method of preparing these data for analysis is to add the six P.I.D. scores for each patient, and the six relief scores for each patient, to determine the Sum of Pain Intensity Differences (*SPID*) for each and the Total Pain Relief Score (*TOTAL* or *TOTPAR*), respectively (Brown, Tr. 4882; Smith, Tr. 5420-21). An average score is then calculated for each treatment group on each method of "scoring" analgesic performance, and this is used as a basis for comparing treatments (Beaver, Tr. 5988-89). Obviously, the higher the SPID score, the greater the reduction in pain intensity for a particular treatment. Similarly, the higher the TOTAL score, the greater the pain relief afforded by the treatment.

410. When the investigator wants to determine the question whether a specific dose of a drug (*e.g.*, two tablets of Excedrin) is more effective or faster-acting than a specific dose of a standard (or known) drug (*e.g.*, two tablets of aspirin), it is appropriate to adopt a three treatment study design which compares the performance of each of these two specific dosages and a placebo (Brown, Tr. 8078; Beaver, Tr. 5982, 5987, 6055-56; Forrest, Tr. 8884-85, 8898, 8948-49; Laska, Tr. 10411-12; Moertel, Tr. 5712). Such a "head to head" (or "efficacy") study design enables the investigator to conclude, where a statistically and clinically significant difference is shown, that one treatment was shown to be more effective or faster than the other in that study (Forrest, Tr. 8898, 8948-49; Beaver, Tr. 6055-56; Brown, Tr. 8078; Laska, Tr. 10411-12). In such a study design, one can have confidence in concluding

that the observed difference between treatments did not result from chance or insensitivity of the study design if the results show that one treatment was statistically significantly more effective than the other treatment and that the standard treatment was statistically significantly more effective than the placebo (Laska, Tr. 10411-12).

410a. The dose-response curve (''DRC'') is a graphic expression of the anticipated relationship between drug dosage and biologic response and is usually based on tests of graded doses. The classic DRC for most active drugs is positive: a larger dose produces greater biologic response until a plateau is reached, beyond which incremental increase in dose does not produce any increase in response (Tr. 4849-92).

411. The DRC for an analgesic compound is plotted as follows: a bioassay relating graded doses of the active agent to degrees of analgesia generate a series of individual data for each dosage tested (data point); by averaging the results of observations at each data point, a mean value is obtained for each data point; the mean results are then plotted on a graph (usually the horizontal axis showing dosage, and the vertical, pain relief); and a ''best-fitting'' line is mathematically drawn connecting the data points by the use of least squared analysis. The line so drawn is a hypothetical fitted line (Tr. 4849-92, 5015-22, 5041-47).

412. DRCs obtained through bioassays typically form the basis of relative potency estimates of test drugs compared with a standard drug. As such, DRC is generally accepted by clinical pharmacologists and clinicians as a useful statistical tool which offers best estimates of the indicated doses of a new (or test) drug to be used in place of a known standard drug (a dose-finding tool) (Tr. 4850, 4860-67).

413. Clinical pharmacologists engaged in bioassays of aspirin-order drugs agree that there appears to be a DRC for aspirin. However, its precise shape and slope, including its plateau level and the dosage point where reverse response, if any, begins, is not known. In any event, it is generally agreed among clinical pharmacologists that aspirin and aspirin-order drugs are mild analgesics and their DRCs are predictably shallow.

Since the relationship of increased analgesia to increased dosage is proportional to the log dose, the relatively flat DRC means that a large increase in dosage is required to obtain a relatively small increase in analgesic response (Tr. 4941-46, 4948-53, 8938-43, 9209; CX 514, p. 35364).

414. When experimental drugs are formulated in anticipation of introducing them into the reservoir of medications available to the public, an obvious and critically important piece of information concerning these new drugs is their recommended dosage range (Forrest, Tr. 8871; Laska, Tr. 10405-07; Sunshine, Tr. 9863-65; Forrest, Tr. 8885). The marketer of a new drug must be able to integrate it into the existing stream of treatments in a fashion that allows physicians to know what effects it will produce at various dosage levels (Laska, Tr. 10405-07).

415. "Relative potency" is defined as the dose of a "test" compound necessary to produce equal biologic effects to a known "standard" compound. Relative potency ratio is a ratio of dosages that produce equal effects (Forrest, Tr. 8885, 8893; Brown, Tr. 4850, 4852-55, 4860-62; Beaver, Tr. 5987; Laska, Tr. 10405-06; CX 803, 804, 805). For example, if the "relative potency" of Compound X relative to aspirin is 2.00, it will take double the amount of aspirin to produce the effect equal to a given amount of Compound X; or, conversely, it will take half the amount of Compound X to produce the effect equal to a given amount of aspirin (Laska, Tr. 10405-06; Brown, Tr. 4850). Thus in general if one knows that the relative potency of Compound X to aspirin is 2.00, one knows that 325 mg. of Compound X will give roughly the same effect as 650 mg. of aspirin (Laska, Tr. 10405-06; Brown, Tr. 4850).

416. The inclusion of a "standard" compound, with widely acknowledged effects at known dosages in the statement is a prerequisite in communicating the relative potency of a new compound, since the very concept is based upon performance relative to that of the standard (Brown, Tr. 4850). Thus, a clinician who knows the analgesic effect produced by such standard treatments as 650 mg. of aspirin will be able to substitute 325 mg. of a new compound with a "relative potency" of

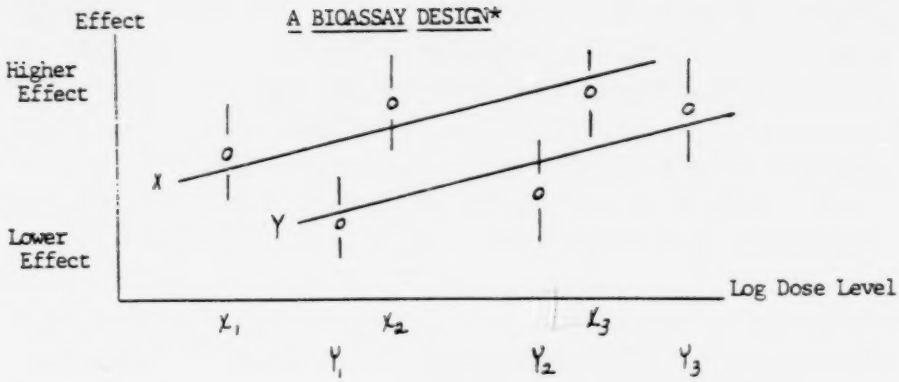
2.00 as against these standard drugs and expect his patients to obtain the same analgesic effect from this new treatment (Laska, Tr. 10405-06; Brown, Tr. 4850-54; Forrest, Tr. 8885). Or, the clinician would be able to substitute 500 mg. of the new compound for 1,000 mg. of aspirin and expect to obtain the same analgesic effect (Laska, Tr. 10416-17).

417. Moreover, use of a relative potency permits a clinician to make an assessment of the risk/benefit ratio in using one analgesic as opposed to another. One has to be able to hold effectiveness constant if any comparison of the relative side effect liabilities of the two drugs is to be made. Without such information obtained from a bioassay, one cannot make that judgment (Beaver, Tr. 5998-99).

418. Therefore, the relative potency of two compounds is not the same as their relative efficacy, because the concept of relative *potency* depends upon holding the level of *effectiveness* of the compounds equal (Laska, Tr. 10417; Brown, Tr. 4853-54). Thus, whereas a "head to head" comparison of the effectiveness of a given dose of an analgesic compound to a given dose of another produces a conclusion about the comparative analgesic *efficacy* of the two compounds at the two stated dosages (F. 410, *supra*), "relative potency" produces a conclusion about the relative *dosages* necessary to produce equianalgesia (F. 419-31, *infra*).

419. The determination of the relative potency of a test compound to a standard compound requires a bioassay, a clinical study of more complex design (using graded doses) than the "head to head" study's single-dose comparison, (Brown, Tr. 4848-49; Forrest, Tr. 8884). A bioassay requires the investigator to compare a *range* of doses of a test compound to a *range* of doses of a standard compound and placebo (Brown, Tr. 4848, 4850, 4852-55; Forrest, Tr. 8884; Laska, Tr. 10417-18). At least two, and frequently three, doses of each compound are generally used, which means that a bioassay may involve five, or seven, or even more treatments (two or three doses of each compound and placebo) (Brown, Tr. 4856, 4872, 8073-76; Beaver, Tr. 5986, 5992-93).

Figure 1.



*Beaver, Tr. 5990-94; Brown, Tr. 4852-55, 4860-62; CX 803; CX 804; CX 805; CX 425Z011

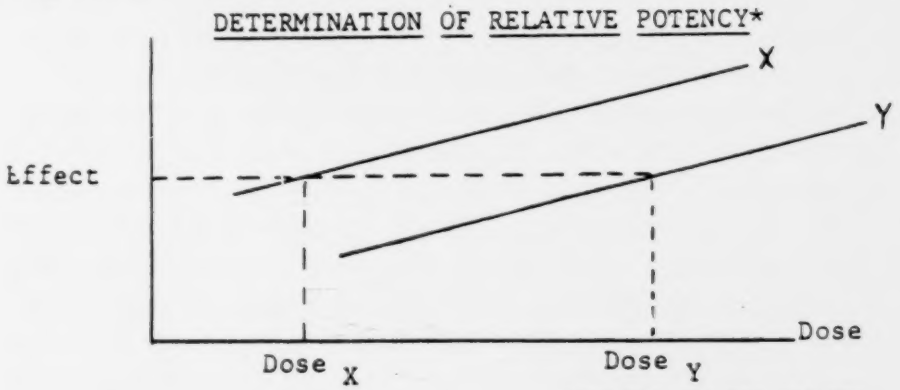
420. In Figure 1 a "best-fit" dose response line for three graded doses of Compound "X" is drawn through the average effect levels for the three successively higher doses of "X" tested (Beaver, Tr. 5988, 5990-94; Brown, Tr. 4860-62). Similarly, "best-fit" dose response line for the three doses of Compound "Y" is drawn through the mean effect levels of the three successively higher doses of "Y" tested (Beaver, Tr. 5988, 5990-94; Brown, Tr. 4860-62).

421. In order to proceed to determine relative potency in this study, several important assumptions about the nature and validity of the bioassay must be satisfied, namely, assumptions of linearity, significant slope, parallelism and equieffective range (Laska, Tr. 10168-73, 10413-16, 10429; CX 900 (graph "a"); Beaver, Tr. 5987-94). First, one must be able to sustain the assumption that each of the "best fit" dose response lines is, in fact, linear. Second, one must be able to sustain the assumption that the two "best fit" dose response lines for "X" and "Y" are in fact parallel. Indeed, lacking linearity and parallelism, a relative potency study has no meaning (Laska, Tr. 10169). Third, one must be able to sustain the assumption that each "best fit" dose response line has a significant slope; *i.e.*, that the level of effect rises, as the dosages increase, to a statistically significant degree (Laska, Tr. 10415). Finally, one must be able to sustain the assumption that

the drugs are performing within an equianalgesic range. Each of these assumptions is tested by appropriate statistical procedure and is sustained only if results are significant at or beyond the 5% level of statistical significance (Laska, Tr. 10413-16). In order for a bioassay to be valid, the "best fit" dose response lines must be linear, positively sloped, parallel and must describe performance of the drugs in their equieffective range (Laska, Tr. 10413-16).

422. The importance of verifying the validity of the bioassay before estimating the relative potency of the compounds is apparent from the fact that the relative potency is simply the horizontal distance between the two dose response lines (Figure 2) (Beaver, Tr. 5987, 5994; Laska, Tr. 10417; CX 900 (graph "a," "b," "c"); Forrest, Tr. 8893-94; CX 803, 804, 805). The ratio of Dose Y to Dose X necessary to produce the *same level of effect* is the relative potency (Forrest, Tr. 8893; Beaver, Tr. 5987; Brown, Tr. 4853; Laska, Tr. 10416-17). Since it represents the horizontal distance between two parallel lines, the relative potency ratio will be the same, regardless of the level of effect chosen, along the entire range of the two dose response lines (Laska, Tr. 10417; Beaver, Tr. 5991).

Figure 2.



*CX 803; CX 804; CX 805; CX 900 (graphs "a," "b," and "c")

423. In bioassays of analgesics, there is a high degree of variability associated with each average effect level of each dosage of analgesic tested (Beaver, Tr. 5988, 5990; Brown, Tr. 4855). This variation is inherent in the subjective response methodology and particularly where mild analgesics are being investigated (Brown, Tr. 4854-55; Forrest, Tr. 8894; Laska, Tr. 10359-64). This results in part from high patient variability in response to the same dose of a compound and shallow slopes of the obtained dose response curves (Laska, Tr. 10360). The fact that OTC analgesics have shallow-sloped dose response curves means that there will be relatively little increase in effect as the level of dosage increases (Forrest, Tr. 8905-07). Stated another way, in order to produce a small increase in effect, a relatively large increase in log dose is required (see CX 514, p. 35364).

424. The variation in individual patients' responses is depicted graphically in Figure 1, as the vertical bars crossing each average level of effect (CX 804, 805; Beaver, Tr. 5988). In a bioassay, where it is essential to draw linear dose response curves which "best fit" the data (F. 420, *supra*) and to determine the horizontal distance between them (F. 422, *supra*), it is equally essential that the amount of variation in the data upon which the "best-fit" lines are based be taken into account (Forrest, Tr. 8894; Brown, Tr. 4868). When relative potency is determined, the level of variation in the data is expressed in a confidence interval that permits a reader to know the range in which the relative potency estimate calculated from one bioassay might vary, up or down, upon repeated measurements (Forrest, Tr. 8894; Brown, Tr. 4868-69). Typically, scientists and published articles discussing such bioassays do so in terms of a "best estimate of relative potency," with an associated 95% confidence interval, with an upper and lower limit (Brown, Tr. 4868-69; Forrest, Tr. 8894).

425. The qualification of all relative potency ratios as "best estimates" is a scientific necessity reflecting the fact that a bioassay provides only a statistically obtained "best fitting" dose response line for each compound tested (F. 420-23,

supra; Laska, Tr. 10418-20). The "true" relative potency of one compound relative to another can be obtained only through repeated bioassays, each producing its own "best estimate" with its own level of precision (Brown, Tr. 5146-47). The indicator of each estimate's precision is the "confidence interval" that surrounds it (Brown, Tr. 4868-69). For example, it is possible that a bioassay's "best estimate" of relative potency will be 4.0; but if the 95% confidence interval associated with that "best estimate" is 2.00, on the lower end, to 8.00, on the upper end, it means that on 100 repetitions all that can be said is 95 of those "best estimates" will fall somewhere between 2.0 and 8.0 (Sunshine, Tr. 9687-88; Brown, Tr. 5140-46). Therefore, the wider the confidence interval, the less precise the relative potency estimate (Brown, Tr. 4869). To take an extreme case, where the confidence interval surrounding a "best estimate" ranges from 0 at the lower end to infinity at the upper end (Brown, Tr. 4869), it would be meaningless and would not permit any conclusions to be drawn about relative potency of the two drugs studied (Brown, Tr. 4869-71).

426. To further illustrate, if the relative potency of a new test compound relative to aspirin is estimated to be 4.0, with a 95% confidence interval of 2.0 on the lower end to 8.0 on the upper end, one could state that, according to the best estimate based on the bioassay, about 160 mg. of the test drug may be expected to provide the same effect as a 650 mg. standard dose of aspirin (F. 416, *supra*), and at the same time that, at 95% confidence level, it might take as little as about 80 mg. or as much as about 325 mg. of the test drug to produce the effect equal to 650 mg. dose of aspirin (Forrest, Tr. 8894).

427. A striking illustration of the imprecision inherent in estimated relative potency obtained from a bioassay is provided by a clinical study where the investigators deliberately used morphine as both the standard compound and the test compound. In that case, the investigators were not interested in estimating the relative potency of an unknown test to a standard compound, but wanted to demonstrate the soundness of the bioassay methodology (Brown, Tr. 5005, 5008-09). In

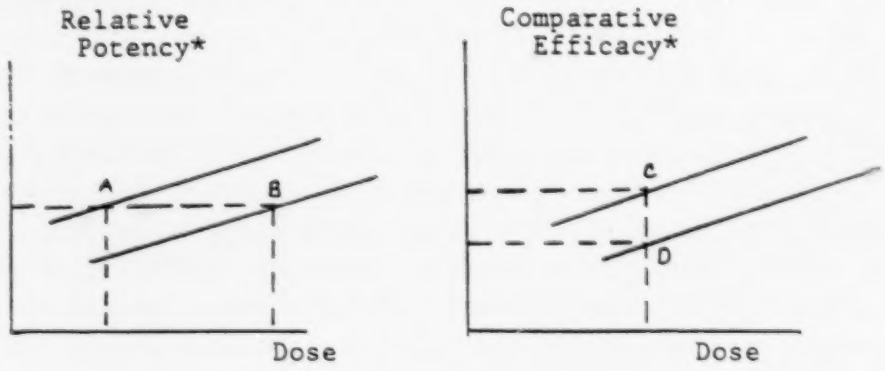
that study, the "true" relative potency was of course 1 (morphine to morphine). Yet, the bioassay yielded a relative potency of .90, with a 95% confidence interval of .44 on the lower end to 1.8 on the upper end (Brown, Tr. 5008-09).

428. The degree of precision of a relative potency estimate obtained from an analgesic bioassay has an important bearing upon the confidence that a scientist can have as he attempts to apply it to clinical situations. The wider the confidence interval surrounding the best estimate, the greater the range of possible equally effective dosages of the test compound relative to the standard. Some clinicians may feel comfortable using the "best estimate" only if the width of its associated confidence interval is no greater than some "reasonable" span, based upon their previous experience (Forrest, Tr. 8913-14). Some may contend that the width of the confidence interval surrounding the "best estimate" that they will accept before they act on it depends upon the purpose for which the drug is to be used or upon the characteristics of the drugs (Laska, Tr. 10206-08). Yet others may take the more liberal view that they will act on the basis of the "best estimate" regardless of the width of its associated confidence interval so long as the interval is not infinite (Sunshine, Tr. 9670, 9689). In any event, it is clear that the relative potency estimate in each of these circumstances provides a convenient and useful device to the clinician which enables him to make a judgment about the dosage of a new drug that will produce effects about equal to those of a known standard drug.

429. Thus, the function of a relative potency estimate obtained from a bioassay is that of dose-finding. As such, a relative potency estimate is not a statement of the *comparative effectiveness* of the drugs (Forrest, Tr. 8886-8907; Laska, Tr. 10487; Sunshine, Tr. 9693-95). This is not to say that the results of a bioassay cannot be used to arrive at conclusions about the comparative efficacy of the drugs studied (Forrest, Tr. 8885, 8894-8907; Laska, Tr. 10437-38). This point was illustrated by Dr. Forrest and agreed to by Dr. Laska, respondents' expert witness (Forrest, Tr. 8885-8907; CX 834; Laska,

Tr. 10487). A graphic depiction of the difference in analysis, one focusing on relative potency and the other on comparative effectiveness, appears in Figure 3.

Figure 3.



*F. 422, supra

*CX 900 (graph "e");
Laska, Tr. 10437-38

Relative potency, reflecting the distance between A and B, expresses the estimated equianalgesic doses of the two drugs, and is measured on the horizontal axis. On the other hand, comparative efficacy, reflecting the distance between C and D, expresses the difference in analgesic effect produced by an equal dose of the two drugs studied, and is measured on the vertical axis (Forrest, Tr. 8899; Laska, Tr. 10437-38, 10487; CX 900 (graph "e")).

430. When two drugs are equipotent (*i.e.*, where their relative potency is 1.00), their dose response curves lay one atop the other (Laska, Tr. 10426, 10430; CX 900 (graph "d"); Forrest, Tr. 8900). When two parallel dose response curves coincide, the horizontal distance between them is 0, as is the vertical distance (Laska, Tr. 10426; Forrest, Tr. 8900). Thus, when two drugs are equally potent, they are also equally effective (Laska, Tr. 10426-27).

431. Where the issue to be determined is *comparative* efficacy (whether the recommended dose of one drug is more

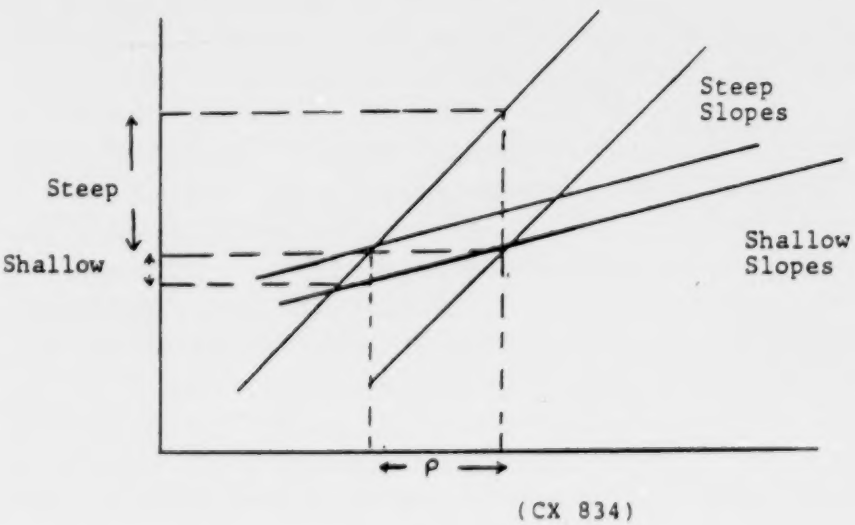
effective than the recommended dose of another), the results of a bioassay need to address the question of whether one can be statistically confident that a difference in their effectiveness exists (Forrest, Tr. 8899-8902; Brown, Tr. 8078). A "head to head" study addresses this question by determining whether the observed difference in effectiveness of the dose of each drug rejects the null hypothesis that there is no difference between the two (F. 410, *supra*).

432. A bioassay can also be used to test a null hypothesis of no difference in effectiveness between the treatments (Laska, Tr. 10426-27, 10519-25; Forrest, Tr. 8899-8902; Brown, Tr. 8078). Graphically, such a test is designed to determine whether one can be statistically confident that the two dose response lines do not coincide (Forrest, Tr. 8899-8902; CX 834). Statistically, such a test asks whether one can be statistically confident that the estimated relative potency is above 1.00 (Forrest, Tr. 8899-8901; Brown, Tr. 4934-35, 4939, 5137-38; Sunshine, Tr. 9688-90; Laska, Tr. 10519-25). Unless one can be confident that the dose response curves do not coincide, one cannot reject the possibility that there is no difference in efficacy between the two (Forrest, Tr. 8899-8902; Laska, Tr. 10425-27). Such a test consists of inspecting the 95% confidence interval that surrounds the estimated relative potency. If that confidence interval embraces 1.00, then one cannot reject the possibility (at the 5% level of confidence) that the drugs tested are equally potent and equally effective (Forrest, Tr. 8899-8901; Brown, Tr. 4934-35, 4939, 5137-38; Sunshine, Tr. 9688-90; Laska, Tr. 10426-27, 10519-25). Examining the 95% confidence interval around the "best estimate" of relative potency to see if it includes 1.00 is analogous to testing whether there is a statistically significant difference in the efficacy of the compounds at the 5% level (Laska, Tr. 11358). Unless the 95% confidence interval *excludes* 1.00, it cannot be said that there is a statistically significant difference in their effectiveness at the 5% level (Forrest, Tr. 8899-8902).

433. As Dr. Forrest testified, and as Drs. Laska and Sunshine, both respondents' experts, agreed, knowledge of the estimated relative potency of two compounds does not impart in-

formation about the magnitude of difference in their comparative efficacy. That their relative potency is 2.00 does not mean one is twice as effective as the other (Forrest, Tr. 8886-8907; CX 834; Laska, Tr. 10487; Sunshine, Tr. 9690-95). In fact, Dr. Forrest demonstrated that where the parallel "best fit" dose response curves of the drugs are shallow, for any given difference in relative potency one would find little difference in the efficacy of the two compounds, but, when the curves are steep, given the same relative potency one will find a substantial difference in effectiveness (Forrest, Tr. 8905-07; CX 834). Thus, as Figure 4 (CX 834) shows, for a given relative potency (horizontal distance between two dose response lines) one can have either very little, or a large, difference in efficacy (vertical distance between the lines), depending on the steepness of the slope. The parameter that governs the relationship between relative potency and comparative efficacy is the slope of the dose response lines (Forrest, Tr. 8905-07; Laska, Tr. 10487), and in studies of mild analgesics the slopes are shallow or relatively flat (Laska, Tr. 10360, 10414, 10464; CX 514, p. 35364).

Figure 4.



(CX 834)

434. An estimated relative potency ratio obtained from a bioassay therefore does not by itself provide sufficient information about the precision of that estimate to enable a person to conclude that the drugs studied are, or are not, equally effective, nor does it provide information concerning the magnitude of difference in their effectiveness. Dr. Finney, in his seminal treatise on bioassay, lists as a prerequisite to accurate reporting, the requirement to supply data on the precision of the "best estimate" reported (Laska, Tr. 10506-08). Information on the precision of the estimate supplied by the 95% confidence interval is important to clinicians because, without that information, clinicians cannot make an informed judgment as to what dosage levels of new drugs may be prescribed to obtain effects equal to those of known drugs. As Dr. Laska testified, this dosage-setting application is by far the most prevalent use of bioassays (Laska, Tr. 10405-07, 10428). However, when the results of a bioassay are to be adapted for use in making the wholly separate determination—is there a statistically significant difference in the effectiveness of two analgesics?—then the information supplied by the 95% confidence interval is essential (F. 432, *supra*; see Laska, Tr. 11347-48). If the 95% confidence interval overlaps 1.00, then the study does not reject, at the 5% level, the proposition that the analgesics are equally effective. If, and only if, the 95% confidence interval excludes 1.00 can one conclude that there is a statistically significant difference in the effectiveness of the recommended dosages of the analgesics studied (Forrest, Tr. 8899-8901; Laska, Tr. 10426-27, 10519-25; Brown, Tr. 4934-35, 4939, 5137-38; Sunshine, Tr. 9688-90).

435. Dr. Louis Lasagna published an article entitled "Effect of Naloxone on the Analgesic Activity of Methodone in a 1:10 Oral Combination" in *Clinical Pharmacology and Therapeutics*, Vol. 15, No. 6, 1974 (Tr. 9721). In this article, Dr. Lasagna used the results of a bioassay study design to test the hypothesis that two compounds were equally effective. In the article, Dr. Lasagna concluded that because the 95% confidence interval around the best estimate of relative potency em-

braced 1.00, his study did not demonstrate a difference in effect (Tr. 10519-22).

436. The analgesic bioassay methodology posits that variability in pain relief response among test subjects does not affect the validity of a bioassay, but rather its precision, namely the confidence limits obtained (Tr. 5033-34). For this reason, it is thought to be appropriate to eliminate subjects with mild or slight pain in order to increase the statistical power of a bioassay (Tr. 5432). Dr. Sunshine testified that while there is a big difference between severe and moderate pain for the individual test subject, for evaluative purposes the only difference will be in terms of SPID scores (Tr. 9733-34, 9754).

437. Dr. Sunshine testified that he is unaware of any correlation between initial pain and any other initial variable such as age, sex, type of delivery, type of anesthetic (Tr. 9726) and has been unable to find any consistent difference in pain relief between those in moderate and those in severe pain (Tr. 9655, 9733). He would conclude, therefore, that it is just as easy for a patient in severe pain to move the three points from severe to zero as it is for the patient in moderate pain to move the two points from moderate to zero (Tr. 9733).

438. On the other hand, it is also thought appropriate in bioassays of mild analgesics, such as aspirin and aspirin-order drugs, to exclude subjects with extreme pain. For example, Dr. Moertel and Dr. Smith agree that in studies of post-partum patients the shorter the post-delivery period the less effectively all tested medication performed (Tr. 5649-50, 5433-34). Some post-surgical patients will not respond to aspirin in the first 24 hours because the severity of the injury overwhelms the aspirin order drug (Tr. 11705-06; BMF 952).

439. From the foregoing (F. 436-38), two observations may be made. *First*, a significant imbalance in the baseline pain (or initial pain) among treatment groups can seriously distort the pain relief scores for treatment groups and thereby lead to false or misleading conclusions of relative potency. This observation is equally valid in cases where such baseline imbalance remains after randomization procedure is followed.

440. *Secondly*, the applicability of a relative potency estimate obtained from a bioassay of subjects whose baseline pain varied from mild to moderate to severe, to the population with mild pain is highly doubtful since two analgesic drugs having relative potencies of above one may in fact be equally effective for the relief of *mild* pain. This observation is valid unless the bioassay studied enough subjects with *mild* pain so that the average pain relief scores of the mild subgroup can be meaningfully compared in order to determine whether the same ratio holds true for *mild* pain (Tr. 5040-44).

441. Statistical significance is an effort to reduce to an acceptable minimal level the likelihood that a particular result is due to chance, but the absence of statistical significance does not necessarily mean that there is no difference (Tr. 9696).

443. Clinical pharmacologists generally determine the sensitivity of an analgesic bioassay model by its ability to differentiate the standard drug (usually aspirin) from a placebo (F. 389, *supra*).

444. In cases where a clinical pain study capable of differentiating aspirin from a placebo fails to show statistically significant difference between aspirin and a test drug, two inferences are possible: (1) that there is no statistically significant difference between aspirin and the test drug, or (2) that whatever difference there may exist is not significant enough to be differentiated by the study model used. In either event, it is reasonable to conclude that the two drugs are about equally effective for all practical purposes.

445. On the other hand, in cases where sound pharmacological reasoning, especially when coupled with a number of clinical studies showing some difference, suggests that there might be difference between the standard and test drugs, some clinical pharmacologists are inclined to attribute the failure to show statistically significant difference to the insufficient sensitivity of the test model. However, that assumption, rational as it may be, remains to be proven by future clinical trials with more sensitive methodology (Tr. 5081, 5979, 7953, 8087, 9006-07; CX 514, p. 35481). In the absence of well-controlled

clinical studies showing statistically significant difference, the claim remains unsubstantiated.

446. For example, in discussing the Bufferin studies submitted to the DESI panel Dr. Beaver stated: "So all one could possibly get out of these three studies in relation to the speed of onset claim, is that these medications will be given to a substantial number of people, and they didn't see any difference, but no one on the panel was so naive as to assume that either individually or together these three studies proved there was no difference. The Lasagna & DeKornfeld Study (see BMF 661) did not show that there was no difference between Excedrin and aspirin but only that they did not find any difference (Tr. 12006). The Lasagna Naloxone article and the Kruskal Encyclopedia of Statistics confirm that "lack of statistical significance at a conventional level does not mean that no real effect is present. It means only that no real effect is clearly seen from data." (Tr. 10360-61).

447. In a bioassay study, if the lower limit of the relative potency estimate is greater than 1, clinical pharmacologists assume, for dose-finding purposes, that there are significant differences in efficacy along the entire range of doses (Tr. 8903, 8949).

448. "Statistical significance" does not necessarily mean "clinical significance." Generally speaking, clinical pharmacologists determine clinical significance of a statistically significant difference by certain clinical standards, such as the magnitude of the difference shown and side effects. However, there is no clear agreement among clinical pharmacologists regarding specific standards. See *e.g.*, Tr. 8902-03.

449. For example, Dr. Forrest testified that he would like to be able to infer clinical significance from a given statistically significant value but has been unable to get agreement among his peers (those clinical pharmacologists who are knowledgeable in the area of clinical testing) (Tr. 8943-45, 9147). He would accept as clinically significant, statistically significant differences if obtained by several researchers (Tr.

8945) and he would accept, as clinically meaningful, what consumers agree is clinically significant (Tr. 9144).

450. However, the term "clinical significance" is also used in a nontechnical sense by practicing physicians, on the basis of individual judgment in their clinical practice. What clinicians usually do is to "eyeball" the difference observed in a clinical study and form a pragmatic judgment as to whether the test drug is preferable or worth trying for his patients, namely whether the difference reported is "clinically significant" in his professional opinion as a physician. Some clinical pharmacologists involved in comparative testing of oral analgesics make clinical judgments based upon the best evidence available from clinical trials and use whatever information they have as a basis for clinical judgment (Tr. 10210-24, 10240-47, 10423-28, 10461-62).

451. Reserved.

452. Practicing physicians use relative potency estimates in order to determine what one medication is needed to obtain the same effect as another. When treating individual patients, they will consider all the available evidence, even where confidence levels embrace one, weigh the possible risks and on that basis reach a decision regarding what medication to prescribe (Tr. 9803, 10244).

453. Among biostatisticians, and clinical pharmacologists trained in analgesic bioassay studies, there is a school of thought that does not insist on statistical significance at the conventional 95% confidence level (P 0.05). With respect to relative potency estimates, they do not insist that the null hypothesis of equipotency be rejected at the 95% level. Generally speaking, the higher the confidence desired, the wider the confidence intervals. The lower the confidence, the narrower the intervals (Tr. 4868).

454. According to the International Encyclopedia of Statistics, by Kruskal and Tanur, an authoritative compendium by recognized in the field, "probably the most common significance levels are .05 and .01, ... but *special circumstances* may dictate tighter or looser levels. In evaluating the safety of a drug to be used on human beings, one might impose a sig-

nificance level of .001. In *exploratory* work, it might be quite reasonable to use levels of .10 or .15, in order to increase power. What is of central importance is to know what one is doing and in particular to know the properties of the test that is used." (Tr. 10205-06) (emphasis added).

455. According to Finney, " 'by adequate precision' [of an estimate of relative potency] is meant a deviation of the estimate from the true value, almost certainly too small to be of any practical importance in affecting any action to be based on the assay." (Tr. 10253). This is certainly the case when relative potency estimates are being used for dose-finding purposes. Even for dose-finding, it is agreed that more precision is required when the drug might be ineffective or toxic at either end of the dose range (Tr. 10221).

456. In a bioassay study, if the lower limit of the relative potency estimate is significantly different from 1, then it is proper to assume that there are significant differences in efficacy along the entire range of doses (Forrest, Tr. 8901, 8949). Dr. Brown testified that a lower confidence limit greater than 1 will reject the null hypothesis of equipotency (Tr. 8126).

457. In hypothesis testing, to determine that the relative potency is statistically significantly greater than 1, the lower confidence limit should not embrace 1 at the 95% confidence level (Tr. 8926-27) (RMF 1061).

458. Dr. Brown testified that data reported as having indeterminate or infinite confidence limits cannot be usefully reported to obtain an estimate of relative potency, but that, with finite confidence limits, a meaningful conclusion can be drawn. However, Dr. Brown, along with Dr. Forrest, published data and conclusions in his article entitled "Clinical And Statistical Methodology for Cooperative Clinical Assays for Analgesia" that appeared in *Clinical Pharmacology and Therapeutics*, even though the confidence limits obtained were infinite (Tr. 4871, 5009).

459. The upper confidence interval of relative potency estimates becomes especially important in a study of a drug highly toxic at high dose levels in view of the toxicity danger to human subjects (Tr. 10222-24, 10207).

460. Drs. Brown and Forrest in their naproxin article reported their results "with reasonable confidence" even though the confidence limits were indeterminate and embraced 1 (Tr. 5117-21). The Brown/Forrest naproxin study produced infinite ("non") confidence limits for each medication in each hospital and when pooled the limits became finite but still embraced 1 and were "fairly wide," "seven-fold" (Tr. 5121). Notwithstanding that even the pooled confidence limits embraced 1, and did not reject the hypothesis of equipotency (Tr. 5123), Drs. Brown and Forrest estimated the relative potency "with reasonable confidence." (Tr. 5127). Dr. Brown explained his use of the term "reasonable confidence" in the naproxin article by saying "the confidence intervals are of the length one ordinarily [finds] those assays." (Tr. 5124-25).

461. Dr. Brown testified that if the lower confidence limit is below 1, as he found in his analysis of the Emich Study, the data cannot reject the null hypothesis of equipotency. However, when his program error was pointed out and the lower confidence limit rose above 1, he claimed that the difference was of little "practical consequence" and a matter of judgment and opinion (Tr. 8125-26).

462. Dr. Laska testified that the fact that a lower confidence limit falls below 1 is not of a practical consequence in the context of mild oral analgesics since it is the estimate of relative potency that clinical pharmacologists use and accept (Tr. 10240-41).

463. The wide fiducial (confidence) limits found in many oral analgesic studies indicate low statistical power. The reasons for these wide limits include high between-patient within-dose variability, the small sample size and small slopes of the dose response regression. (Tr. 10321).

464. Complaint counsel have agreed that reputable scientific journals on occasion publish studies with P values (confidence limits) greater than 0.05 (Tr. 5460-61), and Dr. Moertel will consider data with a confidence level of $P = .065$ as borderline (Tr. 5659-60).

465. The learned journals in the field of biomedical sciences as a rule adhere to the 95% confidence level of statistical

significance. The FDA generally requires, in New Drug Applications, that efficacy and safety be demonstrated at the 95% confidence level. Biostatisticians and clinical pharmacologists generally adhere to the same level of confidence.

466. On the basis of the record as a whole, it is found that, for the purposes of showing that a comparative efficacy or safety claim for an OTC analgesic product is scientifically proven or established, no lesser standard should be accepted.

C. It Has Not Been Established That Excedrin Is A More Effective Pain Reliever Than Aspirin Or Any Other OTC Analgesic

1. *The Ingredients in Excedrin*

467. Each Excedrin tablet contains four ingredients: aspirin (3 grs.), acetaminophen (1.5 grs.), salicylamide (2.0 grs.) and caffeine (1.0 gr.) (F. 2, *supra*). The fact that Excedrin contains four ingredients does not establish its superiority over aspirin or any other nonprescription internal analgesic (F. 400, *supra*).

468. Salicylamide has not been established as an effective analgesic (Beaver, Tr. 6050). The FDA OTC Analgesic Panel confirmed that further well-controlled clinical studies of the compound must be performed to demonstrate that salicylamide alone has adequate and consistent analgesic activity. The Panel concluded that salicylamide is ineffective in currently recommended doses of 300 to 600 and has not been adequately tested for safety. Therefore, it placed the drug in Category III (CX 514, p. 35441). The FDA Panel also stated that "there are insufficient data to determine that salicylamide is either safe or effective when used in combination as an OTC analgesic in the currently marketed dosage of 97.2 to 400 mg." (CX 514, p. 35439). The Panel classified as Category III combinations of aspirin or acetaminophen with salicylamide because there is "insufficient information to determine the safety and effectiveness of salicylamide as an adjuvant. . ." (CX 514, p. 35442). Category III was defined as a classification for which the available data are insufficient to permit final

classification as either Category I (generally recognized as safe and effective and not misbranded) or Category II (not generally recognized as safe and effective or misbranded) (CX 514, pp. 35347-48).

469. Caffeine is not an effective analgesic. The FDA Analgesics Panel so concluded and placed it in Category II as an analgesic (CX 514, p. 35482; Beaver, Tr. 6050). Moreover, the effect of caffeine as an adjuvant to aspirin or acetaminophen has not been established (Forrest, Tr. 9107). After a careful review of the literature and data submitted by drug firms, the Panel concluded that more clinical studies need to be done to show that caffeine contributes to the claimed analgesic adjuvant effect (CX 514, pp. 35483, 35485). Therefore, the FDA OTC Analgesics Panel classified the adjuvant effect of caffeine as Category III (CX 514, p. 35484).

470. Two editions of the *AMA Drug Evaluations* (CX 512 and 518), a reliable and well recognized text on drug therapy (F. 223, *supra*), found no evidence that caffeine in the amounts present in a combination product like Excedrin has any effect on analgesic activity (CX 512I; CX 518G).

471. The Medical Letter (CX 510), a reliable and well-recognized publication (F. 227, *supra*), reviewed evidence concerning the addition of caffeine to aspirin, and found that it had never been adequately demonstrated that the addition of caffeine to analgesics produced any difference in analgesic effect (CX 510).

472. Respondent's Medical Director, Dr. Lanman, relied upon a study by Booy *et al.*, published in Holland in 1975 and translated into English, as support for its position on the adjuvant effect of caffeine in analgesic combinations. The Booy study was performed over a two-day period on outpatients with pain from tooth extraction, and it purported to show enhanced analgesia with an acetaminophen/caffeine combination product (Lanman, Tr. 11515-18; 12066). In fact, this purportedly enhanced analgesia was only apparent on the first day of the study (Lanman, Tr. 12080). On the second day, the combination (with caffeine) apparently performed *poorer* than the acetaminophen alone (Lanman, Tr. 12080; CX 514, p.

35484). The authors made no finding of statistically significant results on either day's data (Lanman, Tr. 11524-26). The authors presented their data in a manner that obscured potential differences in the performance of the compounds studied (Lanman, Tr. 12068). The data as reported by the authors may have resulted from any number of performance results of the compounds with and without caffeine. In fact, the data reported by the authors cannot reject a proposition that there was no difference in the performance of the compounds, or that the compound without caffeine actually performed better than the compound with caffeine (Lanman, Tr. 12069-82; CX 904; CX 905; CX 906). Because of the authors' failure to report any statistically significant results in their study, the reversal on the second day of the first day's favorable trend, and the highly ambiguous way in which the results were reported, permitting the data to be interpreted either as supportive or contradictory to respondent's position, the Booy study cannot be given any weight with respect to the issue of caffeine's adjuvant effect. The Booy study was considered by the FDA Panel on OTC Analgesics as part of its review which led to the conclusion that there are insufficient data to support the adjuvant effect of caffeine (F. 469, *supra*; CX 514, p. 35484; Lanman, Tr. 12213).

473. Respondents also offered a recent study by Wojcicki *et al.*, published in Poland and translated into English, as support for its position on caffeine. This was in part an outpatient study, and one of the two groups under study suffered from common headache (Lanman, Tr. 11513, 12088). This study purported to confirm the results of the Booy study. Like the Booy study, however, the authors of this paper failed to report any test of the statistical significance of their results (Lanman, Tr. 11526). Moreover, from the published report one cannot judge the adequacy of controls employed to assure the blinding in the study (Lanman, Tr. 12083-84). Most important, the authors analyzed and reported the results in terminology different from that used in the study (Lanman, Tr. 12084-91). For example, outpatient subjects were asked to fill in the results of treatment as "pain disappeared," "pain markedly reduced,"

"pain unchanged" or "pain worse" (Lanman, Tr. 12084). The authors reported the results, without any explanation, as "no more pain," "pain greatly improved," "pain slightly improved" and "pain unchanged" (Lanman, Tr. 12084-85). It is possible, as Dr. Lanman speculated, that subjects' "pain markedly reduced" responses were split into "pain greatly improved" and "pain slightly improved," although, from the questions asked subjects, there was no such gradation employed (Lanman, Tr. 12085-86). The same problem is repeated on data gathered from inpatients, *i.e.*, the data reported do not correspond to what the authors say they asked on the questionnaire (Lanman, Tr. 12087-91). Bristol-Myers obtained from Dr. Wojcicki, and offered in this case, statistical analyses purporting to show statistical significance of his findings. However, by his own analyses, the study could not differentiate 1,000 mg. of aspirin, an admittedly effective dose, from placebo (Lanman, Tr. 12091-95). The reliability of the Wojcicki study, therefore, is subject to serious doubt. In another context, Dr. Elvers, Bristol-Myers' Associate Medical Director, took the position that the presence of a significant difference between aspirin and placebo is a "mandatory prerequisite towards the drawing of any meaningful conclusions" from an investigation of clinical analgesia (Lanman, Tr. 12093).

474. For all of these reasons, the Wojcicki study cannot be considered a well-controlled study or a reliable authority and is entitled to little weight on the issue of whether caffeine adds to the analgesia of aspirin and acetaminophen.

475. Respondent also relied on a recent blood level study by Dahanukar, published in an Indian journal as support for its position on caffeine (Lanman, Tr. 11518-19). The study was limited to 12 subjects (Lanman, Tr. 11519). The study did not measure the comparative effectiveness of compounds with and without caffeine (Lanman, Tr. 11519). Blood level studies have not been accepted as evidence of degree of analgesia because no relationship between blood levels and degree of analgesia has been established (F. 401, *supra*). This study therefore is entitled to little weight on the issue of the potentiating effect of caffeine.

476. Respondent also relied upon a study by Houde and Wallenstein wherein the authors concluded that "the results with caffeine must be considered equivocal, although it is possible that dosage may be an important factor, and caffeine may simply be ineffective at much below the 60 mg. dose" (Lanman, Tr. 11523). In fact, this study was presented to the FDA Panel on Analgesics, which concluded that it was the only "well-controlled clinical study to determine whether aspirin plus caffeine is more effective than aspirin alone, and the results of this study are equivocal" (Lanman, Tr. 12065; CX 514, p. 35483). Even though the FDA Panel considered this study, its equivocal results and the absence of other sound evidence still led the Panel to put caffeine in Category III as an adjuvant (F. 469, *supra*).

477. None of the four studies offered by respondent either alone, or in combination, are adequate support for the proposition that caffeine adds to the analgesia of aspirin and/or acetaminophen. At best, the studies produced ambiguous results (F. 472, *supra*), reported results in a manner inconsistsnt with the way data were generated (F. 473, *supra*), failed to incorporate tests of statistical significance (F. 472-73, *supra*), were unable to differentiate an effective dose of aspirin from placebo (F. 473, *supra*), produced equivocal results (F. 476, *supra*), or did not even measure pain relief (F. 475, *supra*).

478. The nature and quantity of ingredients in an analgesic product is not evidence that can establish its superiority to other analgesic products (F. 400, *supra*). In fact, an Excedrin tablet contains only 4.5 grains of ingredients established as Category I analgesics (3.0 grains of aspirin and 1.5 grains of acetaminophen) as compared to the standard 5 grain aspirin tablet. It contains 3 grains of ingredients (2.0 grains of salicylamide and 1.0 grain of caffeine) which the FDA OTC Analgesics Panel has classified as either Category II (ineffective) or Category III (insufficient evidence concerning efficacy or adjuvancy) (F. 468-69, *supra*). In this light, Excedrin can be said to contain a lower amount of proven analgesic ingredients than a plain 5 grain aspirin tablet.

2. *Bioassays of Excedrin and Aspirin*

479. Respondent has admitted representing that Excedrin is a more effective pain reliever than aspirin (F. 272, *supra*). As primary support for its claim, it relies on the results of studies performed on Excedrin and aspirin which, in its expert witnesses' view, adequately support that claim.

480. The Emich Study (CX 425), a bioassay study of post-partum pain conducted in 1968, the Smith Study (CX 453), another post-partum pain study conducted in 1970-1972, and the Sherman Study (CX 439), a pain threshold study of electrical-shock induced dental pain, are in evidence. Three other post-partum pain bioassays offered by Bristol-Myers were rejected, for the reason that Bristol-Myers failed to comply with administrative law judge's long-standing pretrial disclosure directions regarding medical-scientific studies to be offered at trial and that Bristol-Myers failed to show good cause for excepting the studies in question from those requirements (Tr. 9624-41). The three rejected studies are RX 164 for identification (Sunshine Study designated 16H9), RX 165 for identification (Sunshine Study designated 9T1) and RX 148 for identification (Emich Study and data designated W1409). The administrative law judge's modified ruling regarding RX 166 for identification (Sunshine Study designated 10G-12G) would have permitted Bristol-Myers to reoffer it after further interview and cross-examination of Dr. Sunshine regarding that study by complaint counsel, and Bristol-Myers chose not to do so (Tr. 11393-400, 11616-18). Summary and analytical tabulations related to the excluded bioassays were likewise rejected. Bristol-Myers was permitted to make an offer of proof regarding all of the excluded material, which are contained in the excluded exhibit binder of the record. Furthermore, Bristol-Myers' expert witnesses were permitted to refer to, but not to discuss the details of, the excluded studies in explaining their opinions, especially opinions regarding the so-called "pooled data" (See F. 526-28, *infra*).

481. In this connection, it is noted that Bristol-Myers did not include any of the four bioassay studies (RX 148, 164-166 for identification, in the rejected exhibit binder) to the FDA OTC

Analgesics Panel among its submissions in support of its claims of "extra strength" for Excedrin (Lanman, Tr. 12116-17). Dr. Sunshine, who was involved in the conduct of these studies, did not call their results to the attention of the American Medical Association when he was asked in 1971 to comment on a draft of *AMA Drug Evaluations*, which discussed the comparative efficacy of Excedrin and aspirin (Sunshine, Tr. 9702-06). The authors of the Emich Study (CX 425), which included Fred Mueller of Bristol-Myers Statistical Services department (CX 425A), which did not refer to the rejected studies in the introduction to their report, purported to review the available information on Excedrin's efficacy as an analgesic (CX 425G).

a. *The Emich Study (CX 425)*

482. The Emich Study (CX 425) is a bioassay which compares three doses of Excedrin (1, 2 and 4 tablets) to three doses of 5 grain aspirin (1, 2 and 4 tablets) and placebo. The study included 269 female patients all suffering from post-partum pain. It began in 1968 at the Philadelphia General Hospital under the general direction of Dr. John Emich (Sunshine, Tr. 9611). Dr. Emich was an obstetrician and gynecologist, but not a clinical pharmacologist (Sunshine, Tr. 9603). Apparently, Dr. Emich had not done any bioassays before 1968, and was initiated into the techniques of analgesic bioassay by Dr. Sunshine (Sunshine, Tr. 9604-06). The authors concluded that the study showed that tablet for tablet, Excedrin is a more potent analgesic than aspirin for post-partum pain (CX 425V).

483. There was no separate protocol specifically designed for the Emich study that set forth, in advance, the design, treatments, sample size, and statistical analysis to be employed. However, Dr. Sunshine provided Dr. Emich with a copy of a protocol (BMRX 161) that had been developed for use by Dr. Sunshine in 1962 for his own studies of Bristol-Myers' analgesic products (BMRX 161, 162; Sunshine, Tr. 9612, 9617, 9620). Assuming that Dr. Emich used the Sunshine protocol, it is evident that he did not follow it. For example, the Sunshine protocol called for use of patients with surgi-

cal and fracture pain as well as obstetrical patients (BMRX 161A); the Emich Study was confined to obstetrical patients (CX 425H). The Sunshine protocol called for patients entered onto the study to be free from analgesic medication for the five hours preceding initiation of the study (BMRX 161A); the Emich Study eliminated patients who received analgesics during the previous six hours (CX 425H). The Sunshine protocol calls for a cross-over design, with each patient receiving more than one treatment (BMRX 161A, BMRX 162); the Emich Study was a single dose study, in which no patient received more than one treatment (CX 425H). The Sunshine protocol called for a sample size of 200 subjects (BMRX 161B); the Emich Study tested 269 subjects (CX 425H). The Sunshine protocol called for interviews of patients to extend over a four-hour period after administration, with the first interview at one-half hour after administration (BMRX 162); in the Emich study patients were interviewed over a five-hour period after administration of the treatments, with the first interview at one hour after administration (CX 425K). The Sunshine protocol calls for a statistical analysis on "the summary variable of all the hourly relief scores" (BMRX 161B); the statistical analysis of the Emich Study employed, in part, less than all the hourly relief scores (F. 499, *infra*).

484. Dr. Laska, Bristol-Myers' expert witness, analyzed the data generated by the Emich Study through the use of a bioassay computer analysis program. RX 181A-F comprise the computer printouts of that analyses, according to six different variables: percent SPID at 5 hours, SPID at 5 hours, percent SPID at 4 hours, SPID at 4 hours, TOTAL at 5 hours, and TOTAL at 4 hours. The relative potency estimates (rho) for Excedrin to aspirin and the associated confidence intervals at 95% confidence level, based on RX 181, are as follows (Tr. 10174-85):

Variable	5 hrs.		4 hrs.	
	Rel. Pot.	Conf. Int.	Rel. Pot.	Conf. Int.
Percent SPID	2.6	1.1-94.3	4.0	$1.4\text{-}4.8\times10^{5}$
SPID	4.08	$1.3\text{-}3.84\times10^{24}$	7.1	0-infinite
TOTAL	2.27	.86-255	2.32	.85-1230

Based on his computer analysis, Dr. Laska expressed an opinion that the Emich Study provided "compelling evidence of superiority" of Excedrin to aspirin, in terms of pain relief provided at equidoses (Tr. 10185).

485. It should be noted, however, that, out of the two "standard" or "orthodox" analyses of SPID and TOTAL (Brown, 4908, 5086, 5106), only the SPID analysis shows statistical significance at the 5% level of confidence (or $p < .05$) whose confidence interval does not enclose 1. Thus, only the SPID analysis is able to reject the hypothesis that Excedrin and aspirin produce equal effects at 1, 2 and 4 tablet doses (F. 484; Brown, Tr. 4908, 5105; Sunshine, Tr. 9663).

486. In the Emich Study, the relative potency estimate for Excedrin to aspirin on a tablet for tablet basis is 4.02, with a lower 95% confidence interval of 1.4 (Tr. 9659). Dr. Sunshine testified that the results of the Emich Study as expressed by % SPID-4 are "strong scientific evidence that Excedrin is stronger and more effective than aspirin on a tablet for tablet basis." (Tr. 9660).

487. The relative potency of Excedrin to aspirin on a tablet for tablet basis in the Emich Study ranges from 2.27 to 7, with 4 of the 5 parameters significant at the 95% level and 2 having confidence intervals above 1 (Tr. 9660).

488. On January 16, 1968, the statistical department of Bristol-Myers prepared a "final report" of the Emich Study (Tr. 10613-14). That report included the data transmitted by Annette Williams' letter of December 3, 1968 on approximately 230 patients (Tr. 10614). On January 30, 1969, Annette Williams sent the data for an additional 44 patients of the study to Bristol-Myers for analysis (Tr. 10614). Despite Bristol-Myers' belief that the Emich Study had concluded with 225 patients, it nonetheless included these final 44 in its final analysis as presented in Atlantic City. It could have discarded those final cases and considered the Emich Study terminated at 225 patients (Tr. 10615). It would have been proper for Bristol-Myers to discard the results of the last 44 patients of the Emich Study, thereby increasing the strength of the conclusions one could draw based on the Emich Study (Tr. 10619).

489. The relative potency estimate of Excedrin to aspirin for the variable SPID-4 is 7.1, with a 90% confidence interval from 1.97 to 1.44 (Tr. 10183; BMRX 181D). The estimated relative potency of Excedrin to aspirin in the Emich Study using variable total 5 (TOPAR) is 2.27, with a 90% confidence interval from 1.02 to 24.1 (Tr. 10184). The estimated relative potency of Excedrin to aspirin for the variable total 4 (TOPAR) is 2.32, with a 90% confidence interval of 1.01 and 36 (Tr. 10184). The Emich Study results for the response variables SPID-4, TOTAL-5 and TOTAL-4 have lower confidence limit values above 1 at the 90% level of confidence (Tr. 10184-85).

490. The Emich Study is flawed by a problem that compromises its fundamental validity. Despite the fact that subjects were purportedly assigned to the seven treatments in the study through a randomization technique, more patients in "severe" initial pain were assigned to the Excedrin treatments than to the aspirin treatments (Brown, Tr. 5174; Sunshine, Tr. 9662). This procedure resulted in an imbalance in the baseline pain levels between the Excedrin groups and aspirin groups, before any tablet was ingested, that were large enough to be statistically significant at the .02 level (Brown, Tr. 4903, 4921; Forrest, Tr. 8960; Laska, Tr. 10199). Statistically significant imbalances in initial pain levels among treatment groups at baseline is a serious problem that cannot be ignored (Laska, Tr. 10621; Forrest, Tr. 8960-61, 9090-91; Brown, Tr. 4904-05, 4911, 5083-84, 5093-94, 5100, 8029). Respondent's expert, Dr. Laska, agreed that he would not have confidence in using data from the conventional SPID analysis of the Emich Study due to this baseline pain imbalance (Laska, Tr. 10440, 10487-88).

491. The level of baseline pain (*i.e.*, pain prior to medication) is the single most important variable influencing the response to analgesics (Beaver, Tr. 5968; Brown, Tr. 8053, 8113, 8118-23, 8128-34). Indeed, the authors of the Emich Study themselves note that in their study "the response of an individual patient to a given medication was closely related to her starting pain level" (CX 425N). Although several experts

of Bristol-Myers expressed the view that post-study correction or adjustment of the baseline imbalance problem by the use of percent SPID (as was done in the Smith Study) was not unusual, it is questionable whether such after-the-fact statistical "correction" can reasonably be expected to cure the defect and restore the validity of a flawed analgesic study to that of an unflawed one (Brown, Tr. 8113-14, 8136, 8050-53, 8060-61).

492. It is fair to say that where statistically significant baseline pain imbalance results after randomization, the result is the same as in a nonrandomized study in that the attempted control of patient assignment bias failed. In fact, in the Emich Study the assignment of larger numbers of patients in "severe pain" to the Excedrin treatments created a bias favoring Excedrin (Brown, Tr. 4094, 4936, 5174; Sunshine, Tr. 9734). The bias results from the fact that Excedrin had the opportunity to relieve more pain in more patients than aspirin did (Brown, Tr. 4904, 5174). Excedrin had more opportunity to reduce pain intensity and to provide pain relief than aspirin, because patients in the Excedrin group on the average started with more pain (Brown, Tr. 4904; Sunshine, Tr. 9734). As the authors of the Emich Study observed: "Patients who had severe pain at the outset proved to receive significantly more relief on the average than those complaining of less discomfort" (CX 425"O").

493. The practical consequence of the statistically significant baseline pain imbalance among the treatments in the Emich Study is that it reduces confidence in the study, and all its results, to a point where it cannot be accorded full weight (Forrest, Tr. 8960-62, 9090-91, 9116-17; Brown, Tr. 4905, 4911-14, 4916-17, 4928, 5100, 8149-50, 8154-55). The fact that there was a statistically significant imbalance on baseline pain — perhaps the most important of all variables that influence the results of pain relief studies — raises the specter of bias in patient assignment (Brown, Tr. 4911, 4921; Forrest, Tr. 8960-62, 9091). The record shows that the chance of a true randomization producing the baseline pain imbalance present in the Emich Study is only two (2) times out of 100 (Brown,

Tr. 4903, 4921; Forrest, Tr. 8960). Respondent's expert witness, Dr. Laska, agreed that if subjects were not assigned to treatments in an unbiased fashion, the entire study would be seriously compromised (Laska, Tr. 10590-94). While after-the-fact numerical transformations of the data may be the only plausible way to address this central problem statistically, no statistical "correction" can address the issue of whether patients were, in fact, assigned to treatments in an unbiased fashion (Brown, Tr. 4911-12, 5092-93, 8143-44; Forrest, Tr. 8960-61). Dr. Forrest, an eminent authority in the field of analgesic bioassays, and Dr. Brown, an expert biostatistician experienced in analgesic bioassays, concluded that the serious baseline pain imbalance present in the Emich Study diminishes the study's weight to a point where they would not rely on it as credible evidence regarding the issue of whether the superiority of Excedrin over aspirin has been scientifically established (Forrest, Tr. 8960-61, 9121-23; Brown, Tr. 8108, 8149-50, 8154-55).

494. The position of Drs. Forrest and Brown regarding the weight to be accorded the Emich Study is corroborated by the fact that apparently only one published analgesic study has been found where the authors reported statistically significant differences in initial pain levels among the treatment groups (Laska, Tr. 10626-27). Dr. Louis Lasagna, the author of that article, is a respected and well qualified clinical pharmacologist (Beaver, Tr. 5903), whom Bristol-Myers cited in support of its position in its 1968 Comments to the Federal Trade Commission in a Trade Regulation proceeding involving OTC analgesics (Laska, Tr. 10626, 12023-24; Sunshine, Tr. 9721). What Dr. Lasagna concluded regarding that study was that, because of the bias introduced by the statistically significant differences in starting pain levels, he could not come to conclusions about the performance of the tested drugs (Laska, Tr. 10626-27).

495. Reserved.

496. The authors of CX 425 do not report that patients varied in terms of their initial pain to a statistically significant degree (Brown, Tr. 5174; CX 425). However, the authors do out-

line a technique of analysis, called "Percent SPID," which they say adjusted the "SPID" scores so they were "freed . . . from the influence of starting pain levels" (CX 4250). The authors of CX 425 do not report the estimate of relative potency based either on "SPID" or "TOTAL" (Brown, Tr. 4906-07). The relative potency they reported was based on their "% SPID" analysis. However, the purported "protocol" for the study (BMRX 161B) did not mention "% SPID."

497. Respondent's experts, Drs. Sunshine and Laska, contend that the use of the % SPID analysis in the Emich Study successfully "corrects" the problem introduced by the existence of statistically significant baseline pain imbalance (Sunshine, Tr. 9659, 9662, 9671; Laska, Tr. 10199-200). However, they did not say that the use of an adjustment for the SPID score (*i.e.*, the use of "% SPID") also corrects what may be the same problem with the other summary variable analyzed in the Emich Study, namely "Pain Relief" (CX 425R; F. 406-07, *supra*). In fact, Dr. Smith, the author of the Smith Study, testified that in his study, even though there was no statistically significant imbalance in starting pain levels, he "tried a variety of correction terms to eliminate any potential bias owing to the fact that starting pain does, in fact, influence pain relief as it influences pain intensity difference" (Smith, Tr. 5421).

498. "% SPID" is a technique developed by the authors of the Emich Study for purposes of *post hoc* analysis of the data. The normal "SPID" score for each patient is expressed as a proportion of the maximum possible "SPID" score that each patient could have obtained (CX 425K, L). Respondent's expert witness, Dr. Laska, pointed to a general source as support for the type of correction provided by the "% SPID" technique. However, Dr. Laska was unable to cite any published article where the author used % SPID or any other statistical device to correct baseline pain imbalance (Laska, Tr. 10626). Dr. Sunshine, who claimed that baseline imbalances occurred frequently in studies during the 1960's, cited no article that employed an analysis on the % SPID variable or any other

"correction," and he admitted that he had not used % SPID in any of his published studies (Sunshine, Tr. 9717-20, 9746).

499. Bristol-Myers' experts analyzed the results of the Emich Study at four and five hours after administration of the treatments (Sunshine, Tr. 9659; BMRX 181C, D, F). Dr. Laska testified that the four-hour analysis is meaningful because both Excedrin and aspirin recommend a four-hour interval between doses (Laska, Tr. 10548-49). The analysis of "% SPID," "SPID" and "TOTAL" at the four-hour period is a *post hoc* analysis outside the purported protocol's specification that the summary variable analysis cover "all the hourly relief scores" (BMRX 161B; Laska, Tr. 10540-41, 11292-93). When he was asked why he had not, for example, analyzed the summary variables in the Emich Study based on data from three-hour or even two-hour observations, Dr. Sunshine answered that "you can do anything you want . . . It depends what you're looking for" (Sunshine, Tr. 9707). Respondent's expert Dr. Laska admitted that in his published work, and in that of Dr. Sunshine, when the summary variables "SPID" and "TOTAL" were analyzed *all* of the data generated in the studies were included (Laska, Tr. 10548-51). Analysis of a data segment not laid out in advance in the protocol, is a data massaging that destroys the validity of the analysis" (Moertel, Tr. 5543).

500. Even if one were to dismiss the gravity of the baseline pain imbalance problem and accept the % SPID "correction," the Emich Study is equivocal. Out of the six variables analyzed by Bristol-Myers' experts, only four will give an unbiased estimate of the relative potency because the uncorrected SPID analysis (SPID-5 and SPID-4) is infected with a quantitative bias introduced by the initial pain imbalance (Laska, Tr. 10440, 10487-88; Sunshine, Tr. 9662, 9671). Of that four, two have estimates of relative potency with confidence intervals that embrace 1.00 (RX 181E-F; Tr. 10183-84). Thus, accepting all of respondent's "corrections" and *post hoc* analyses, only two of the four parameters in the Emich Study analyzed by respondents, which could give an unbiased estimate of relative

potency, reject the hypothesis that Excedrin and aspirin are equally effective.

501. The Emich Study was submitted for publication in the *Journal of Clinical Pharmacology and Therapeutics*. The authors were asked by Dr. Modell, the Journal's editor, to comment on the generalizability of the study results to pain etiologies other than post-partum. They answered that the issue was irrelevant (CX 910). Their study was not published (Lanman, Tr. 12095-97).

b. *The Smith Study (CX 453)*

502. The Smith Study (CX 453) is a bioassay which, like the Emich Study, investigated three doses of Excedrin (1, 2 and 4 tablets), three doses of aspirin (1, 2 and 4 tablets) and placebo (Smith, Tr. 5393). The study was funded by Bristol-Myers and involved 785 female patients (about three times the sample size of the Emich Study) suffering from post-partum pain at the Boston Hospital for Women (Smith, Tr. 5392-93). The study was conducted during the period commencing in the fall of 1970 through January 1972 (Smith, Tr. 5392) under the direction of an experienced, reputable investigator, Dr. Eugene Smith, of the Harvard Medical School and Massachusetts General Hospital (F. 59, *supra*).

503. The protocol for the Smith Study was reviewed and approved by the Research Committee of the Massachusetts General Hospital to ensure that the study followed scientifically appropriate and accepted procedures (Smith, Tr. 5393-94).

504. The primary purpose of the Smith Study (CX 453) was to investigate not only the efficacy of Excedrin but the influential variables that may affect clinical trials generally and to develop a method of investigation and to study the relative potency of Excedrin (Tr. 5445).

505. The Smith Study was well-designed, employed the appropriate controls, and suffered from none of the problems which characterized the Emich Study (Brown, Tr. 8150). All significant variables were satisfactorily balanced across treatment groups (Smith, Tr. 5434, 5506-07). Moreover, all meth-

ods of analysis employed in the study yielded consistent results: none of the analyses showed statistically significant differences at the tested dose levels between Excedrin and aspirin at the .05 level (Smith, Tr. 5422-24); all of the analyses produced relative potency estimates between 1.1 and 1.3 with lower 95% confidence limits around .50 to .70 (F. 506-08, *infra*).

506. The results of the Smith Study are:

Parameter	Estimate of Relative Potency	Lower Confidence Limit	Upper Confidence Limit
TOTAL4	1.36	.51	7.3
%SPID5	1.25	.69	2.57
SPID5	1.13	.54	2.64
%SPID4	1.33	.7576	2.78
SPID	1.22	.59	3.04
TOTAL5	1.2	.45	4.35

(Tr. 10294-95) (BMRX 182).

507. Data generated in the Smith Study were analyzed for the five-hour period over which the study ran (Smith, Tr. 5413). The relative potency estimates for Excedrin to aspirin, are 1.13 based on "SPID-5," with 95% confidence limits of .54 to 2.64 (BMRX 182B; Laska, Tr. 10294), and 1.2 based on "TOTAL-5," with 95% confidence limits of .45 to 4.35 (BMRX 182E; Laska, Tr. 10294). Neither of the two conventional analyses rejects the null hypothesis that Excedrin and aspirin are equally effective because the lower 95% confidence intervals enclose 1.00 (Smith, Tr. 5423; Laska, Tr. 10426-27; Brown, Tr. 4933-35; Forrest, Tr. 8963-65; Sunshine, Tr. 9751). Thus, neither analysis reflects a statistically significant difference between Excedrin and aspirin at the .05 level at the tested dose levels (Smith, Tr. 5422-24).

508. Dr. Laska, Bristol-Myers' expert, also analyzed the results of the Smith Study using the % SPID method. Since there is no baseline imbalance on initial pain in the Smith Study, and therefore no bias for using % SPID to "correct" it, the results according to % SPID-5, not surprisingly, closely parallel the results of the normal SPID-5 analysis (Brown, Tr.

4936, 8144-45). The relative potency estimate based on % SPID-5 was 1.25, with 95% confidence limits of .69 to 2.57 (BMRX 181A; Laska, Tr. 10294). The four-hour data analyzed by respondent is also consistent with the five-hour data analysis. The "best estimate" and associated 95% confidence intervals for SPID-4, % SPID-4 and TOTAL-4 were, respectively: 1.22 (95% limits of .59 to 3.04) (BMRX 181D); 1.33 (95% limits of .75 to 2.78)(BMRX 181C); and 1.36 (95% limits of .51 to 7.27) (RX 181F). (See Laska, Tr. 10294-95). Each of these four analyses produces a relative potency estimate with a 95% confidence interval well below 1.00. Thus none of them show a statistically significant difference between Excedrin and aspirin at the .05 level at the tested dose levels. Indeed, the data from the Smith Study, however analyzed, cannot reject the hypothesis that aspirin is more potent than Excedrin at the tested dose levels (Laska, Tr. 10518). The results from the Smith Study are quite consistent with the results that would be obtained in a bioassay where the *true* relative potency of the two compounds was, in fact, 1.00 (Brown, Tr. 5009, 8157-58).

509. The Smith Study showed that for mild pain, the relative potency of aspirin compared to Excedrin is 2.3, with infinite confidence intervals due to the small sample size (Tr. 10301) (BMRX 182).

510. The Smith Study is a more precise and reliable estimate of the relative potency of Excedrin to aspirin than is the Emich Study (Laska, Tr. 10537). It suffered from no methodological flaws that compromised either its reliability or its weight (Brown, Tr. 8150). Moreover, it employed more subjects than the Emich Study (785 vs. 269). 785 is a large sample for bioassay studies of this kind (Forrest, Tr. 8965). Dr. Beaver referred to sample sizes in analgesic studies of 675 to 750 patients as "gigantic" (Beaver, Tr. 6023). Dr. Sunshine indicated that 30 patients per treatment would be a "ballpark" minimum adequate sample size, and having 50 patients per treatment group would be "wonderful" (Sunshine, Tr. 9773). The Smith Study had about 100 patients per treatment (Forrest, Tr. 8964). Generally, the larger the sample, the easier it is to show differences between the two compounds, if there are in

fact differences (Forrest, Tr. 8965). The fact that Dr. Smith is a well-known researcher adds to the reliability of his study (Brown, Tr. 8150). For all of these reasons relating to the precision, sample size methodological elegance, the results of the Smith Study should be accorded greater weight than the Emich Study regarding the issue of whether Excedrin's claimed superior efficacy over aspirin has been scientifically established (Moertel, Tr. 5597; Brown, Tr. 8150).

511. Respondent has "pooled" the results of the Emich and Smith Studies in order to produce yet another analysis of their results. Essentially, "pooling" is a statistical device that combines the "best estimates" of relative potency, together with other data bearing upon the variability in each study, and produces a "pooled" estimate, with a new set of 95% confidence limits (Laska, Tr. 10319-50; Forrest, Tr. 8965-74). However "pooling" the Emich and Smith Studies data does not create a new, well-controlled study, whose results can be used to establish a claim of superior efficacy. It may be said that pooling reduces the two independent Emich and Smith Studies to one "pooled" study (Forrest, Tr. 8965-68; Brown, Tr. 8159-63). In order to establish a scientific proposition, one needs replication of the statistically significant results of one study by another study (F. 370, *supra*). What is required is at least two well-controlled clinical studies which demonstrate statistically significant differences between the compounds tested. Pooling does not meet that requirement (Forrest, Tr. 8967-68; Brown, Tr. 8161).

512. "Pooling" combines the results of several studies to arrive at an overall conclusion of relative potency estimates on the basis of available data, across a variety of studies, investigators and locations (Tr. 10186-99, 11312-13).

513. The information pooled includes the relative potency estimates, sample sizes, slopes, sums of the squares and the confidence limits, intervals and values (Tr. 10193).

514. The rationale for pooling is to use all available information in an attempt to obtain an overall estimate of what the true relative potency is (Tr. 10188-89).

515. Finney would restrict pooling of "assays in which different species of animals have been used as subjects or different measurements have been taken as responses or experimental techniques have been fundamentaly different. . . ." (Tr. 10335). In pooling data from more than one hospital, Finney would calculate the relative potencies for each hospital and then pool them using the Bennett method (Tr. 8969).

516. Dr. Laska testified that data from different investigators can be pooled so long as they are collected in a reasonably similar way and/or if the several studies are conducted under the same or similar circumstances. For example, subjective response studies would not be pooled with animal or experimental pain studies. Further support for this proposition is seen in the Naloxone Article by Dr. Lasagna (Tr. 8970, 10196, 10324).

517. Dr. Laska testified that he finds support for the pooling of all the Excedrin studies in Bennett ("Combining Estimates of Relative Potency and Bioassay") and Armitage ("Point and Interval Estimation in the Combination of Bioassay Results") (Tr. 10337-40).

518. According to Dr. Laska, pooling is permissible when: (1) the estimate of relative potency for each of the studies is within the confidence intervals of both of them or (2) when one of the estimates of relative potency is within both intervals and the upper limit of one study is below the estimate of the other (Tr. 11306-08).

518a. Dr. Forrest's VA co-op study pooled data from the several hospitals, including data with infinite limits to obtain one relative potency estimate with finite confidence limits (Tr. 5010-11).

519. In cases where the validity of a relative potency etimate is sufficiently demonstrated by a well-controlled bioassay whose findings are then replicated by another well-controlled bioassay by an independent investigator, the rationale for pooling the data from the two studies with those of others which are flawed and/or fail to show significance at reasonable confidence levels, is difficult to understand to a layman.

520. However, absent two or more well-controlled studies confirming the validity of a relative potency estimate, pooling may be a statistically acceptable device for obtaining a composite estimate on the basis of available information if one must come up with a relative potency estimate. This is akin to the pragmatic approach by which clinicians not well versed in analgesiology assess analgesic bioassay reports (F. 450, *supra*).

521. The pooled results of the Emich and Smith Studies are:

Parameter	Estimate of Relative Potency	Lower Confidence Limit	Upper Confidence Limit
%SPID5	1.58	.99	3.05
%SPID4	1.82	1.12-3	3.88
SPID5	1.67	.95	4.06
SPID4	1.97	1.08	5.92
TOTAL4	1.65	.86	5.03

(Tr. 10311, 10313-14) (BMRX 63).

522. The % SPID-5 pooled result of Emich and Smith rejects the null hypothesis at a confidence level of P = .10 or 90% (Tr. 5155).

523. In order for the lower confidence limit of the pooled Emich and Smith Studies to rise above 1, the P-value would have to be approximately .06 to .08 (Tr. 10314-15) (BMRX 63).

524. According to Dr. Laska, a reanalysis of the Smith data by baseline pain level shows relative potency estimates (Excedrin to aspirin) of: 2.3 for mild pain, 1.3 to 1.5 for moderate pain, and 1.6 to 1.8 for severe pain. The relative potency estimate for mild pain (2.3) had infinite confidence intervals due to the small size of the subsample. The confidence intervals for relative potency estimates for moderate and severe pain were undetermined (Tr. 10301-02; BMRX 182).

525. Dr. Laska testified that, based on his reanalyses of the Emich and Smith data, when combined, they show that for moderate pain the relative potency of Excedrin to aspirin is 1.26, with 95% confidence intervals of .54 to 3.51, and for

severe pain it is 1.82, with 95% confidence intervals from .88 to 10.02 (Tr. 10305-06).

526. Dr. Sunshine also referred to two other studies of his own, both of which compared the potency of Excedrin and aspirin, using post-partum pain subjects and the Sunshine protocol (RX 166 and 168 for identification). They were both rejected, but Dr. Sunshine was permitted to refer to them in his answers to the ALJ's questions regarding the applicability of bioassays to moderate pain. The first, Hopper Study (16H9) (RX 168 for identification), used 1, 2 and 4 tablets. The second, Gueria Study (10G1) (RX 166 for identification), used 2/3 of a tablet, 2 and 6 tablets. Both used a modification of the statistical technique used in Emich and Smith, and compared one dose of Excedrin and three dose levels of aspirin (Tr. 9643-45).

527. Dr. Sunshine conducted *post hoc* stratification analyses of the Emich, Smith, Hopper and Gueria Studies in order to determine Excedrin's relative potency for the moderate pain subset of the patient samples and testified that every one of the four studies produced a relative potency estimate of above 1 for the moderate pain subgroup. "1.5, 2, 4, depending on the study. There was variability. But in each and every time, it was greater [than 1]. And . . . if you just average it up, it was one-and-a-half times greater." (Tr. 9784-85).

528. Although Dr. Sunshine's above analyses are interesting, they are of little value, for several reasons. First, setting aside several objections to *post hoc* analyses of subset data, the size of the subset of test patients in the moderate pain group in those studies was clearly inadequate. Dr. Sunshine was emphatic that any subgroup analysis of less than 30 would lead to "distortion" and be incapable of providing any "meaningful data" (Tr. 9769-70). For example, he agreed that the subsample size of less than 17 per treatment in the Emich Study was inadequate for a valid or meaningful *post hoc* stratification analysis of the uterine pain subgroup and suggested that 30-50 would be reasonable (Tr. 9769-73). In the Emich Study, the size of the moderate pain subsample was

less than 15 (Tr. 9719). Dr. Brown also testified that stratification analysis is not valid unless each pain group contained enough subjects and different results showed up (Tr. 5038-40). Further, the Emich Study excluded the mild pain group and no analysis of that study for the mild pain patients is possible. Further questions regarding the applicability of postpartum pain studies to other types of pain have been noted (F. 374-79, *supra*).

529. Dr. Laska introduced a novel analysis of the data generated by the Smith and Emich Studies for the purpose of demonstrating the magnitude of differences in the effectiveness of Excedrin and aspirin (Laska, Tr. 10354-59). Dr. Laska in effect subtracted from the effect level of both Excedrin and aspirin, the effect level of placebo in each study for % SPID-5, and calculated the percentage difference in the remaining effect between Excedrin and aspirin (Laska, Tr. 10358, 10444-45, 10475, 10481-82; CX 900 (graph "e"); CX 901). Applying the novel analysis to the Emich Study, Dr. Laska concluded that Excedrin added about 59% to the effectiveness of aspirin over and above what is supplied by placebo (Laska, Tr. 10358; CX 901). Using the same "Laska" formula, Dr. Laska calculated from the Smith Study that Excedrin adds approximately 10% to the pain relieving effectiveness of aspirin over and above what is supplied by placebo (Laska, Tr. 10358-59; CX 900 (graph "e"); CX 901). The statistical significance of any of these purported differences is not shown.

530. Although complex statistical tests could be performed to test the significance of these percentage differences, Dr. Laska agreed that one could simply use the 95% confidence interval around the best estimate of relative potency on "% SPID-5" to test statistical significance of these percentage differences in effectiveness. If the 95% confidence interval embraced 1.00, then the percentage difference in comparative "% SPID-5" effectiveness of Excedrin and aspirin would not be statistically significant (Laska, Tr. 10468). Using this method, since all estimates of relative potency in the Smith

Study have 95% confidence intervals that embrace 1.00 (F. 507-08, *supra*), all measures of comparative effectiveness of Excedrin and aspirin would not be statistically different at the .05 level. And of the four relative potency estimates in Emich that Dr. Laska would use for this purpose (Laska, Tr. 10440, 10487-88), only two have 95% confidence intervals that do not embrace 1.00 (% SPID-5 and % SPID-4) (Laska, Tr. 10468-69).

531. Nonparametric analysis takes into account repetitive events which lead to the same general conclusion but none of which independently supports a firm conclusion. A nonparametric analysis of Excedrin's strength compared to aspirin addresses the question of how many repeated trials show Excedrin with a relative potency greater than 1. Pooling addresses the issue of the actual relative potency of one treatment to another (Tr. 10189).

532. In nonparametric analysis, the frequency of results showing a relative potency estimate of above 1 is the determining factor. The greater the frequency, the stronger the evidence showing the superiority of one treatment over another (Tr. 10186).

533. BMRX 211 is a graphic representation of the nonparametric analysis of the Emich and Smith Studies showing the estimates of relative potency for each pain condition studied in those tests (indicated by dots), the overall estimate within each study for relative potency (indicated by an X), and the confidence intervals around the estimate of relative potency for each study (indicated by a solid vertical line). BMRX 211B indicates the overall pooled estimate of Excedrin's relative potency (indicated by a circled X) and the 95% confidence interval around that estimate. BMRX 211B shows that Excedrin is superior to aspirin (Tr. 10317).

533a. Nonparametric analysis essentially eyeballs the data generated by a number of studies and attempts to reach an overall observation regarding a general trend either favoring or disfavoring a proposition.

3. *The Sherman Study on Experimentally Induced Dental Pain (CX 439)*

534. CX 439, entitled *Comparison of the Effectiveness of Two Analgesic Agents by Laboratory Testing*, ("Sherman Study"), is the report of an experimental pain study conducted in 1962 for Bristol-Myers, which purported to compare the relative analgesic effectiveness of 600 mg. of aspirin and two tablets of Excedrin on a double-blind basis (CX 439D; Elvers, Tr. 10771). The Sherman Study presupposes a direct correlation between the clinical effectiveness of analgesics and their ability to raise the pain threshold in artificially induced pain, the level of pain intensity at which an experimental pain stimulus is perceived by a subject as first causing pain. In this study, pain was induced by applying electrical shocks to the dental pulp of a selected tooth of test subjects (CX 439N).

535. The Sherman Study was authored by Drs. Harold Sherman, Joseph E. Fiasconaro and Harry Grundfest (CX 439A). Dr. Sherman was a dentist on the faculty of the dental school of Columbia University, and had some experience in clinical testing of anesthetics related to dentistry. Dr. Fiasconaro was a dentist on the same faculty who worked with Dr. Sherman on some of Dr. Sherman's published works in that field. Drs. Sherman and Fiasconaro conducted the experiments. Dr. Grundfest, a respected Professor of neurology at Columbia's College of Physicians and Surgeons, provided neurological assistance to the team (Elvers, Tr. 10761-62). When first approached by Bristol-Myers in 1957, the experience and published work in the area of drug testing of the Sherman-Fiasconaro team was limited to studying the pain-threshold effects of local dental anesthetics by electrical shock method (Elvers, Tr. 10761, 10763).

536. At that time, their methodology using electrical stimulation of dental tooth pulp was incapable of evaluating the performance of mild oral analgesics, which Dr. Elvers admitted was a "far more challenging objective" (Elvers, Tr. 10763-64). After spending several years to adapt their methodology and equipment for use in evaluating mild analgesics, Drs. Sherman and Fiasconaro conducted the study beginning in

1962 without Dr. Grundfest's participation (Elvers, Tr. 10763-64, 10777). Before the testing of subjects began in the study, Dr. Elvers (Bristol-Myers' then Associate Medical Director) informed the investigators that their study might be used to support advertising claims (CX 445A, B).

537. The test subjects in the Sherman Study were dental out-patients and were tested on a single treatment at each test session (Elvers, Tr. 10772-73). At each test session a subject's "baseline" (premedication) pain threshold was determined by measuring the amount of electrical current necessary to elicit the first detectable sensation of pain (*i.e.*, pain threshold), on the basis of an average of readings taken at five-minute intervals for a period of 20 to 40 minutes before the test drugs were given (Elvers, Tr. 10773).

538. Thereafter the test drug was administered and threshold readings recorded at five-minute intervals for up to 70 minutes (Elvers, Tr. 10775). From these readings a "plateau" period was picked by the investigator as the period of maximum post-treatment elevation of the pain threshold, and an average measure of current flowing at the plateau was recorded (Elvers, Tr. 10818).

539. The ability of a test drug to raise the pain threshold was measured in terms of a "percentage elevation of threshold," that is, the percentage increase in electrical current required to reach the post-medication threshold "plateau" over the premedication "baseline" threshold level (Elvers, Tr. 10818).

540. At the conclusion of the study the mean average percentage elevation of pain threshold achieved by a test drug by a subject was calculated (CX 439P), and the average percentage elevation of pain threshold achieved by Excedrin, aspirin and placebo across subjects was determined (CX 439Q).

541. The test drugs used were two tablets of Excedrin, two tablets of 300 mg. aspirin obtained from 4 commercial sources, and placebo (CX 439G). Excedrin and aspirin tablets were left in their commercial form (Elvers, Tr. 10771), except that, after the initial randomization of treatments was completed, unmarked Excedrin (*i.e.*, tablets without the distinc-

tive "E") were substituted for one-third of the scheduled placebo treatments (Elvers, Tr. 10780). Therefore, there were twice as many Excedrin treatments in the study as those for aspirin or placebo (Evans, Tr. 6402; Elvers, Tr. 10814). All treatments were sealed in coded envelopes, and the investigators were instructed to rip open the envelopes and have the subjects swallow the enclosed tablets without anyone looking at the tablets (Elvers, Tr. 10774-76).

542. During a "dry run" of the Sherman Study (without medication), approximately 30% of the initial population was eliminated from further testing because of their reportedly erratic pain threshold readings (CX 439C; Elvers, Tr. 10765-69). The authors of the Sherman Study characterized the dropouts as "placebo reactors" and attributed the absence of placebo effect in their study to the exclusion of placebo reactors (CX 439B-D).

543. The results of the Sherman Study, as reported in CX 439, are as follows: In 65 tests on 14 subjects, Excedrin caused an average elevation of the pain threshold of 15%, with different test subjects' elevations ranging from 2 to 50%. In 48 tests on 15 subjects, the aspirin brands used caused an average elevation of threshold of 2.7%, with different test subjects' elevations ranging from 0 to 12% (CX 439N). From these results the authors concluded that they were able to "establish clearly a difference in analgesic effectiveness" between Excedrin and aspirin (CX 439D) and that Excedrin is more effective than aspirin "in elevating the threshold to electrical stimulation of the dental tooth pulp" (CX 439L).

544. It is generally agreed among the students of analgesiology that experimental pain studies measuring threshold effects are not reliable for the purpose of determining comparative performance of mild analgesics in the relief of pathological pain or pain in natural state (F. 547-49, *infra*). In the Sherman Study the authors note that "it is widely held (for references see Beecher, 1959, Lasagna, 1964) that laboratory tests are unsuitable for characterizing the relative effectiveness of analgesic agents" (CX 439B). They also noted, in another pain threshold study using the dental pulp electrical shock

method published in 1963, that some investigators viewed experimental pain studies as "inaccurate to the point of being hopelessly useless, both as far as offering theoretical insight and as a practical tool for clinical application" (CX 439D; Tr. 10910).

545. In that 1963 article, Drs. Sherman, Fiasconaro and Grundfest compared the threshold effects of codeine and aspirin and concluded that 30 mg. codeine was 3 times more effective than 1800 mg. aspirin (Tr. 10918). This finding is in sharp contrast with the results of clinical pain studies (analgesic bioassays) by Drs. Kantor, Sunshine, Laska, et al., and by Dr. Bloomfield, which suggest that 60 mg. codeine is no more effective than 600 mg. aspirin and possibly too low a dosage to produce reliable analgesia (Elvers, Tr. 10923-24). In CX 439, the authors note that their earlier (1963) study, using the same method adopted in CX 439, was contradicted by the available clinical literature (CX 439B). In this connection, the Sherman Study reported the peak effect for aspirin as occurring at 25-30 minutes (CX 439H), in sharp contrast to the generally accepted aspirin peak effect time of one to two hours based on bioassay studies (Beaver, Tr. 5945).

546. Pain induced by electrical shock on tooth pulp is a fast, jabbing type of pain and is unlike most clinical pain, which is described as dull, throbbing, aching and of much longer duration. Electrical stimulation of tooth pulp has proven to be notoriously unreliable even among experimental pain models (Evans, Tr. 6352, 6359, 6373-74). Fast, jabbing pain involves different physiological mechanisms than clinical pain (Evans, Tr. 6349, 6373-74). Other experimental methods which more closely approximate clinical pain have been shown responsive to standard analgesics such as morphine. With all of their shortcomings, they are more appropriate analogs for clinial pain in the laboratory than the Sherman model (Evans, Tr. 6331, 6338, 6352, 6369, 6373-74).

547. Dr. Beecher, whom Dr. Elvers regards as "the leading man in the field and sort of the father of experimental research and clinical research as well" (Elvers, Tr. 10801), concluded in his treatise, *Measurement of Subjective Responses* (1959),

that although some workers believe it satisfactory, "in view of the remarkable inconclusiveness of the method of electrical shocks to teeth in man . . . it is difficult to accept work that depends upon this method and technique" (Elvers, Tr. 11111). As late as 1978, Wolff, whom Dr. Elvers referred to as "definitely a leader in experimental pain research" (Elvers, Tr. 10800), was still attempting to develop a methodology which would achieve reliable results with electrical stimulation of dental tooth pulp (Elvers, Tr. 11084-88).

548. It has been suggested that the type of pain elicited by electrical stimulation of dental tooth pulp might be unique to itself (Elvers, Tr. 11166). Dr. Mumford, a respected researcher, compared subject reactions to real toothache and pain induced by electrical stimulation of tooth pulp, and concluded that "qualitative assessment" of the real toothache "differed considerably" from the pain induced by electrical stimulation (Elvers, Tr. 11163-64).

549. In their 1963 article, Sherman, *et al.*, recognized that experimental models employing transient ("fast") pain, and those employing dull, throbbing prolonged ("slow") pain, produced "qualitative[ly]" different kinds of pain, which involved different "pain reporting pathways" in the body. They therefore cautioned that analgesics found efficacious using their "fast" pain model "may be more or less so for painful sensations elicited by other pathways" (Elvers, Tr. 11156-57).

550. In CX 450, an earlier draft of the Sherman Study (CX 439), the authors stated that "aspirin might conceivably be more effective [than Excedrin] in relieving other types of pain" than that induced by electrical stimulation of dental tooth pulp (CX 450G). Dr. Elvers, then Associate Medical Director of the Bristol-Myers Products Division, instructed the authors to remove this statement from the report as "gratuitous speculation" (CX 449D; Elvers, Tr. 11159). Nevertheless, the authors still state in CX 439 that their results may be limited to pain involving "pain reporting pathways" similar to those involving electrically stimulated tooth pulp pain (CX 439L), clearly indicating that they recognized the doubtful

generalizability of results using a transient pain model (Evans, Tr. 6409-10).

551. In any event, it is highly doubtful whether a study based on pain threshold performance of an analgesic agent can provide any meaningful conclusions about pain reduction. Certainly the Sherman Study did not (Evans, Tr. 6368). The pain threshold is a transient, momentary point in the pain experience and is not a relevant point in the measurement of clinical pain (Evans, Tr. 6472-73).

552. On the other hand, measurement of the suprathreshold point at which pain is intolerable (tolerance level) has been shown to reliably respond to standard test analgesics such as morphine, and more closely correlates with the type of pain patients report in the clinic (Evans, Tr. 6382-6385). Wolff, in a paper co-authored with Dr. Thomas Kantor and Dr. Eugene Laska, noted in 1969 that "[l]ogically, pain tolerance, being suprathreshold pain, would seem a better index of analgesic efficacy than pain threshold . . ." (Elvers, Tr. 11127).

553. The Sherman Study also failed to employ the appropriate scientific procedure, the so-called "method of limits," in determining pain threshold. The "method of limits" averages the measurement of the *ascending* threshold (the point where a pain stimulus, increasing from subthreshold intensity, is first detected as painful) and the *descending* pain threshold (the point where a pain stimulus, decreasing from suprathreshold intensity, is last detected as painful) in order to correct for the tendency of test subjects to under- and over-shoot actual pain threshold (Evans, Tr. 6377; Elvers, Tr. 11140). Wolff, a highly reputable investigator (Elvers, Tr. 10800), measures both ascending and descending pain thresholds and pain tolerance in studies using electrically induced dental tooth pulp pain (Elvers, Tr. 11145).

554. Sherman's elimination of 30% of his original subject sample because of reportedly erratic threshold readings (F. 542, *supra*) was a totally unacceptable scientific procedure (Evans, Tr. 6395). Since Sherman never gathered data on these subjects, there is no way of knowing the effect their in-

clusion might have had on the results of the study (Evans, Tr. 6395), nor the representativeness of the remaining sample. Beecher suggested that elimination of persons with erratic pain thresholds might leave a sample representative only of itself (Elvers, Tr. 11199). Sherman's inference that those subjects eliminated from the study were placebo reactors (CX 439B-C) was an untested assumption (Evans, Tr. 6393-94), and there is no basis for believing it correct (Evans, Tr. 6393-95). Dr. Laska expressed a similar conclusion (Laska, Tr. 10493-94). Sherman also recognized that the attempted elimination of placebo reactors "raises the possibility of 'tampering' with the data" (CX 439C). One researcher, specifically addressing the Sherman Study, suggested in a published article that those eliminated from the Sherman Study as inferred placebo reactors would actually have had *lowered* thresholds with the aspirin, putting the study's methodology in serious question, in light of aspirin's known effectiveness (Elvers, Tr. 11191-92). Also see FDA OTC Analgesic Panel Report, CX 154, p. 35444.

555. According to Dr. Evans, the zero response rate for placebo reported in the Sherman Study may indicate a breakdown in double-blinding, since the placebo response rate is known to be always above zero in well-blinded studies (Evans, Tr. 6391). According to the Sherman data, placebo actually began to lower the threshold at precisely the time (25 minutes) when other compounds were shown to elevate it (CX 439K, S). The obvious explanation for *lowering* of pain thresholds after administration of placebo is that the subjects were aware of the identity of the test drugs, and when a placebo is given them, responded more sensitively to pain (Evans, Tr. 6406). The fact that Excedrin and aspirin were left in their commercial form also increases the possibility that the subjects may not have been successfully blinded.

556. The raw data for CX 439 is replete with calculation errors (Evans, Tr. 6398, 6402-03). Dr. Elvers agreed that about one-half of Sherman's calculations of percentage elevation of threshold had to be corrected for reanalyses (Elvers, Tr. 11260). Moreover, prior to calculation of baseline thresh-

olds, Dr. Sherman discarded certain readings on the raw data sheets without explanation (Evans, Tr. 6401).

557. Furthermore, the method by which Dr. Sherman selected data points which he believed represented the "plateau" of post-medication elevation was never explained, varied from session to session, and followed no discernible standard or rule (Evans, Tr. 6401-02). Bristol-Myers attempted to address this problem in its reanalyses of underlying data by the so-called "geometric mean peak ratio" technique (Elvers, Tr. 10821; Mueller, Tr. 10092). However, as Dr. Elvers admitted, the "geometric mean peak ratio" technique cannot distinguish between aberrant peak values and true threshold elevations and is not found in the literature (Elvers, Tr. 11237). At any rate, Bristol-Myers' reanalysis of the Sherman data disclosed the inability of the study to differentiate aspirin from placebo at the .05 level of significance (RX 212A, 213A; Elvers, Tr. 11256).

558. The credibility of the Sherman Study is placed in further doubt by the extraordinarily high amounts of electric current recorded as flowing through subjects at the point where pain threshold was reached. According to the data, eight (8) of the fifteen (15) test subjects required amounts of electricity as high as 800, 480, 117.5, 111, 82, 78, 57, and 56.5 microamps before reaching threshold pain (CX 886(a)). The pain thresholds for dental tooth pulp in healthy teeth, as reported in the literature, are normally reached at currents of 1.2 to 26 microamps (Elvers Tr. 11212-13). Dr. Elvers' opinions offered as possible explanations for these abnormally high readings were largely based on speculations (Elvers, Tr. 11217-94).

559. The record shows that Bristol-Myers' subsequent attempt to replicate the Sherman Study (CX 439) was unsuccessful. Bristol-Myers employed Dr. Ozick, now associated with New York University (Elvers Tr. 10900-01), for this purpose. According to Dr. Elvers, the study undertaken by Dr. Ozick for Bristol-Myers was "initially comparable" to the Sherman Study (Elvers, Tr. 10897). Dr. Ozick was unsuccessful in reproducing Dr. Sherman's work using Sherman's methodology (Elvers, Tr. 10898-99), and eventually modified

Sherman's procedures and equipment "in the hope of replicating the Sherman type of study" (Elvers, Tr. 10898-99). Even after these modifications by Ozick, the methodology and equipment were not capable of producing "the stability [Bristol-Myers] felt necessary for the study of analgesics," (Elvers, Tr. 12393). The Ozick Study was abandoned. However, Dr. Elvers testified that Ozick "never set out to replicate the study" (Elvers, Tr. 10900), but was merely trying to develop the method, equipment and competence "that would permit him to attempt a replication of the Sherman Study . . . [and] in that attempt he failed" (Elvers, Tr. 10900).

560. From the foregoing discussion of the Sherman Study (CX 439), it is found that CX 439 may have some limited application to dental pain threshold elevation, but it is unreliable for the purpose of comparing the effectiveness of aspirin and Excedrin in any other pathological pain in the natural state.

D. It Has Not Been Scientifically Established That Speed Of Relief Provided By Bufferin Is Significantly Greater Than That Provided By Plain Aspirin

1. *Claims of Faster Relief and Twice as Fast Relief*

561. As Bristol-Myers argued to the Federal Trade Commission in its Comments on a Proposed Trade Regulation Rule on OTC analgesics filed February 6, 1968, if "one wants to claim that [an] analgesic acts faster on tension headache than some other preparation, *one should be required to prove that it acts faster, i.e., by interviewing people under the proper conditions and finding out how soon the headache goes away*" (F. 375, *supra*; emphasis added).

562. In this proceeding, instead of presenting *studies* done on headaches, Bristol-Myers relied on an argument based on analogy by its Medical Director to suggest that Bufferin's onset of analgesic activity occurs sooner than plain aspirin's (Lanman, Tr. 11619-59). Bristol-Myers' argument in this regard is twofold: (1) that Bufferin is absorbed more rapidly than aspirin into the bloodstream, and (2) that, therefore, Bufferin will start to relieve pain sooner than plain aspirin (Lanman,

Tr. 11635, 11658-59). In support of this argument, a number of "blood level" studies were offered and received. These studies report that Bufferin produces somewhat higher blood levels of hydrolyzed and unhydrolized aspirin than plain aspirin (Lanman, Tr. 11635-58).

563. However, Bristol-Myers' Medical Director, Dr. Lanman, once expressed the same opinion offered by every independent expert who addressed the issue in this proceeding and every expert Panel and publication that has considered it (F. 592-601, *infra*). In an April 1969 memorandum, Dr. Lanman stated:

> It is quite true that aspirin is absorbed more readily from Bufferin than from ordinary aspirin tablets. Unfortunately, it is a much more difficult thing to correlate clinical relief with Bufferin. In fact, we have no such correlation between clinical and laboratory tests and the explanation is a very complex one. (CX 508)

564. In fact, as CX 508 states, no correlation between blood levels of aspirin and onset, degree or duration of analgesia has been demonstrated (F. 410, *supra*). Four of complaint counsel's expert witnesses were examined and cross-examined on this issue, and each of them consistently held to the view that well-controlled, clinical investigation is the prerequisite in order to establish that one analgesic compound relieves pain faster than another (Azarnoff, Tr. 9195, 9225; Forrest, Tr. 8980, 8987-90, 9035, 9043-45; Moertel, Tr. 5800-06, 5817-18, 5860; Beaver, Tr. 5947-48, 5951-52, 5957-58, 5961-64). In defense, respondent offered the testimony of not one independent clinical pharmacologist who supported its position. Only Dr. Lanman, an employee of Bristol-Myers for 19 years, was offered to present that position, and Dr. Lanman's opinion testimony concerning Bufferin's superiority in this proceeding is not consistent with his view submitted to the FTC in 1969 (CX 508) (F. 563, *supra*).

565. The proposition that Bufferin provides higher blood (serum concentration) levels of ASA, SA and TSA sooner than plain aspirin is supported by a preponderance of credible

evidence. Complaint counsel have admitted that studies and tests submitted by Bristol-Myers to the FTC reported that Bufferin is absorbed into the bloodstream faster than aspirin (BMPF 60-107), and that the blood salicylate level of Bufferin 10 minutes after ingestion and 20 minutes after ingestion is in both instances twice as high as that of aspirin (BMF 114-144).

566. The Stough Study that measured the total salicylate in the blood at 0, 10, 20, 40, 120, 240 and 300 minutes after ingestion of aspirin, Bufferin, Anacin and Bayer aspirin (Tr. 11633-34; CX 506Z405), shows that with incremental doses of aspirin there is an incremental increase in blood level. Bufferin provided more aspirin into the bloodstream at 10 minutes than 10 gr. Bayer aspirin, 13 gr. Anacin or 10 gr. plain aspirin and provided more total salicylate at 20 minutes than 10 gr. Bayer, 13 gr. Anacin and 20 gr. aspirin (CX 506Z413).

567. BMRX 157, a graph of the results of the Stough Study, depicts the wide difference in blood level between the administration of 10 and 20 grains of aspirin (BMRX 157; Tr. 11633).

568. Both the Paul Study (CX 786) and the article published by Dr. Sleight in the *Lancet* (a British medical journal) (CX 787) have shown that the level of aspirin produced in the blood by Bufferin is twice that produced by plain aspirin (Tr. 11635-36). Paul reported that the Bufferin formula resulted "in at least a two-fold increase in the blood salicylate levels. The ten-minute salicylate level following [Bufferin] exceeds the twenty-minute salicylate level for ordinary aspirin by more than 20%. Furthermore, the salicylate level twenty minutes after ingestion of [Bufferin] is almost 2-1/2 times the twenty minute ordinary aspirin level." (CX 786D).

569. CX 550, the Stanford Research Institute Study entitled "Clinical and Statistical Studies of Blood Salicylate Levels" was a triple crossover design studying St. Joseph aspirin, Bayer aspirin and Bufferin, all purchased on the open market, through analysis of blood samples taken 0, 10, 20, 45, 90, 125 and 150 minutes after ingestion (CX 550B; CX 550J).

570. CX 550 found that after 10, 20 and 45 minutes, the subjects given Bufferin showed significantly higher salicylic

acid concentrations in the blood than those given either St. Joseph or Bayer aspirin (CX 550J). For example, after 20 minutes the concentrations of total salicylic acid in the blood of subjects given Bufferin were from 68 to 100% higher than those given Bayer or St. Joseph aspirin (CX 550J).

571. The results of CX 550 corroborate the results of blood level studies conducted in Bristol-Myers' own research and development laboratories (BMF 61-107, 114-133, 134-144) which show that Bufferin is absorbed more quickly (from 50-100% more salicylic acid within the first 10 minutes and approximately twice as much after 20 minutes) than plain aspirin (CX 550K).

572. A second study by Stanford Research Institute entitled, "A Clinical and Statistical Study of Blood Salicylate Levels Following The Ingestion of Two Preparations Containing Aspirin" (Tr. 11640-41; CX 506Z174-Z177, Z405-414) was a double-blind randomized comparison of Bufferin and Bayer aspirin in which blood samples, drawn at 0, 10, 20 and 40 minutes after ingestion, were analyzed for salicylic acid (CX 506Z176). At all time periods Bufferin was found to have statistically significantly higher blood levels than Bayer (59-64% higher on the average), results which were consistent with the earlier (CX 550) Stanford Research Study (CX 506Z176).

573. In 1958 Dr. Paul, and during the period 1959 through 1968 Drs. Paul and Routh, compared serum levels of Bayer with samples of Bufferin and found that all of the Bufferin samples showed numerical superiority of Bufferin to Bayer at 10 and 20 minutes after ingestion. The numerical superiority of Bufferin to Bayer found in the 36 studies was significant to $p = .05$ or less in 34 of the 36 studies with 31 having a p value of .01 (CX 506N). And in 1958 Dr. Cronk found that the addition of Di-Alminate® caused a similar enhancement in absorption of salicylate (CX 506M).

574. Dr. Heimer, at Seton Hall College of Medicine and Dentistry, found that Bufferin's higher total salicylate levels (TSA) were statistically significantly higher than those for Bayer up to 120 minutes, Bufferin's free salicylate levels (FSA) were statistically significantly higher than Bayer up to

45 minutes, and the differences between TSA and free salicylate (FSA) were significantly higher for Bufferin at 10, 20 and 30 minutes (CX 506Q; BMRX 136; Tr. 11646-47; BMRX 177D; Tr. 11657).

575. Komoda found in 1965 that Bufferin gave significantly higher TSA levels than Bayer at 10, 20 and 30 minutes (CX 506Q).

576. In 1962, 1963, 1965, 1968, 1969, through measurement of TSA, FSA and ASA, Bufferin was found to have been absorbed faster than Bayer (CX 506Q-R).

577. Truitt and-Morgan found the plasma salicylate concentration for Bufferin "approximately twice as high" as for Bayer at 10, 15, 20 and 30 minutes with the differences being highly significant at $p = .001$ (CX 506R).

578. In 1958, Paul and Routh reported in a study of 10 and 20 minute blood levels for 1, 2 and 3 tablet (5, 10 and 15 grains) doses of Bufferin, Anacin and Bayer that (1) blood levels increased with increasing dosage and (2) Bufferin levels were far superior at each dosage (CX 506S).

579. At 10 minutes the ASA level of plain aspirin is .5 mg/ml compared to 3 mg/ml for Bufferin. At 20 minutes, the comparison is 1 mg/ml for plain aspirin and 3.5 mg/ml for Bufferin. Both of those differences are statistically significantly in favor of Bufferin (Tr. 11649; BMRX 136A; CX 506R footnote 67).

580. The ASA blood levels of Bufferin are significantly higher than those for aspirin at 20 minutes (BMRX 136C; CX 506R, footnote 65; Tr. 11651-52; 11652-53).

581. At both 10 and 20 minutes after ingestion, the ASA blood levels of a 10 grain dose of Bufferin are significantly superior to those for a 10 grain dose of aspirin (Tr. 11652-53; BMRX 136D; CX 506R, footnote 66).

582. There is a twofold or larger increase in absorption rate for TSA comparing Bayer and Bufferin aspirin (Tr. 11654-55; CX 506M; BMRX 177B; CX 523).

583. BMRX 177C, a graph based upon a study by Morgan and Truitt, published in Vol. 54, No. 11 of the *Journal of Pharmaceutical Sciences*, pp. 1640-46 (Nov. 1965) entitled "Evalu-

ation of Acetylsalicylic Acid Esterase in Aspirin Metabolism, Interspecies Comparison" (CX 521A-H; CX 506R footnote 72) shows that the observed TSA concentrations of Bufferin are higher than those for Bayer aspirin (Tr. 1655-56; BMRX 177C): "[T]he aspirin blood levels of [Bufferin] exceed those of a plain aspirin at all of the time periods test[ed] *i.e.*, 10, 20, 30, 45, 90 and 240 minutes." These higher ASA blood levels were comparable with previously reported plasma salicylate levels for [Bufferin]." (CX 521G).

584. Dr. Beaver testified that it is unknown whether the unhydrolyzed aspirin (ASA) or the salicylate (SA) or some combination of the two is, when in solution in the blood, responsible for analgesic activity (Tr. 5942-53). However, there are some studies (one by Dr. Lasagna and one by Dr. Houde) (Tr. 5977) that indicate that aspirin (ASA) is about 1.5 times as potent an analgesic as an equivalent amount of salicylate (SA) (Tr. 5976-77).

585. Dr. Azarnoff testified that both ASA and SA are active principles, that they have different potencies (Tr. 9108) and that ASA is the more active (Tr. 9193). And Dr. Forrest testified that the state of the art is that the active Metabolite in aspirin is ASA (Tr. 9025-27).

586. Dr. Levy, one of the foremost experts in pharmacokinetics, wrote in an article entitled "Aspirin: Absorption Rate and Analgesic Effect," published in *Anesthesia and Analgesia*, November-December 1965:

> There is considerable evidence that aspirin (ASA) is a more effective analgesic than salicylic acid (SA), both in man and in animals. Aspirin in the body is hydrolyzed rapidly to salicylic acid, and it has been found that oral administration of this drug in rapidly absorbable form (aspirin solution) results in higher and earlier maximum blood levels of unhydrolyzed aspirin than are obtained after administration of aspirin in a more slowly absorbed form (compressed tablets). (Tr. 1161-62).

586a. Dr. Beaver testified that unhydrolyzed aspirin (ASA) peaks before one-half hour after ingestion and is rapidly elimi-

nated or biotransformed into salicylate or some combination of ASA and SA (Tr. 5946).

587. Total salicylate (TSA) can be measured by measuring either the sum of unhydrolyzed acetylsalicylic acid (ASA) plus salicylic acid (SA) or by allowing all ASA to hydrolyze and measuring it as SA. The hydrolysis of ASA can be inhibited — to allow measurement of ASA, TSA or SA (Tr. 9236-38).

588. Whether ASA or SA is the active or more active moiety that produces analgesic effect, the studies cited hereinabove show that Bufferin produces higher blood levels of them sooner than plain aspirin. "There is clear experimental evidence based upon well designed blood level studies which substantiate the claim that buffered aspirin is more rapidly absorbed than plain aspirin (Refs. 1-3 [citing Bristol-Myers' blood level data. See BMRX 234; CX 514, p. 35481]). Comparisons of the most commonly used plain and buffered aspirin show that salicylate blood levels are twice as high in the first ten to twenty minutes for the buffered aspirin product compared to regular aspirin. It can be shown that the differences in plasma levels in the first twenty minutes correlate quite well with the amount of drug absorbed (Ref. 4)."

589. Dr. Levy in his article (F. 586, *supra*) stated:

> Differences in gastrointestinal absorption rate have a pronounced effect on the magnitude and time of occurrence of maximum drug levels in the body in the case of drugs (such as aspirin) which are rapidly metabolized and/or excreted. Consequently, absorption rate can affect the onset, intensity, and duration of pharmocologic effects *if* the latter are related to the magnitude of drug levels in the body. Since the absorption rate of drugs administered in tablets can be modified appreciably by the pharmaceutic properties of the tablets, differences in tablet formulation may modify markedly the pharmacologic effect of many drugs. (Tr. 11686-87; emphasis added).

590. It is generally agreed among clinical pharmacologists that the limiting factor governing aspirin's absorption rate is the dissolution rate of the dosage form (tablet) and that the

method of fomulation can significantly affect a tablet's dissolution rate apart from buffering.

591. The FDA Analgesic Panel corroborates that view and recommended a standard dissolution test procedure for buffered analgesic products.

> From the available data, the Panel finds that simply adding buffering agents to aspirin does not generate an increased dissolution rate over unbuffered aspirin. Important factors appear to be the type of buffering agent used and other undefined factors, e.g., tablet compression during manufacturing, etc. . . . For this reason, actual testing of the dissolution rate of buffered aspirin products is necessary to determine if the buffering agent actually does affect the dissolution rate of the aspirin products and to what extent.
>
> Also, the Panel notes that an adequately buffered aspirin product may not have an advantage over a well-formulated unbuffered product. In some studies, unbuffered aspirin performs as well as buffered aspirin products (CX 514, p. 35375; also see pp. 35469-70).

592. While Dr. Forrest agreed with the FDA Analgesic Panel that "The basic problem is that there are no well-controlled clinical studies that unequivocally prove or disprove that these differences in absorption will result in clinically important differences in the onset, intensity or incidence of relief of pain or fever," (Tr. 9024-25; CX 514, p. 35480) he testified that the extrapolation of blood levels to a drug's anticipated effect is a "very rational one" and is used in other fields where there are "objective measures of what is happening." And "the big problem for us here is the subjective nature of this whole problem of pain and pain relief."

593. Dr. Forrest agreed with the Panel's statement that:

> If the blood level time curves were superimposable, it would be reasonable, based on all known studies, to assume that the formulations would have equal onset, duration and intensity of pharmacological effects. However,

> if one product were substantially more rapidly absorbed than the other, one cannot conclude that there is necessarily a corresponding difference in onset of effect. The mathematical relationship between changes in blood levels and corresponding changes in onset, or intensity of analgesia response is not presently known for aspirin. (Tr. 9025-27, 9028; CX 514, p. 35373).

594. Dr. Forrest also testified that the blood level curves for aspirin and Bufferin could not be superimposed without moving the baseline onset point (Tr. 9034-35). He further testified that Bufferin's more rapid early absorption could make the onset of pain relief later or earlier, but that the hypothesis of Bufferin's earlier onset is interesting and possibly correct (Tr. 9036).

595. Dr. Beaver did not claim that there was no relationship between Bufferin's higher blood levels and increased clinical pain relief but only that blood level does not correlate "nicely" or that the correlation is not "simple" or "direct" or that blood levels "may not in any tidy way mirror" clinical effect (Tr. 5952).

596. The FDA OTC Analgesic Panel's conclusion with respect to drug blood levels corroborates the expert opinions reviewed above. The Panel states:

> Aspirin is commonly used as a standard analgesic drug for comparison with other drugs in which assays of blood levels are made rather than direct measurements of the analgesic effectiveness of these agents. The Panel has evaluated this technique and concludes that there is inadequate evidence that the amount of drug in the blood correlates directly with clinical analgesia. The Panel emphasizes that this is not to say that a relationship between blood levels and clinical response does not exist, but rather that the relationship is complex and not presently understood. However, the Panel does recognize that an important value of drug blood level determinations is that they do give an indication of comparative dissolution rates. . . .

> The Panel recognizes that the drug labeling related to the onset, intensity and duration of pharmacologic effects can influence the consumer's selection of a product that can find no convincing evidence to support labeling claims which suggest a faster onset of effectiveness . . . There is also no direct evidence available to the Panel which suggests a greater intensity of analgesia for comparable products . . .
>
> . . .[S]ome buffered aspirins are somewhat more rapidly absorbed from the gastrointestinal tract than unbuffered aspirin and might also be expected to show earlier higher salicylate blood levels. However, the Panel is unaware of any data that demonstrate that buffered aspirin provides a more rapid onset, a greater peak intensity or a more prolonged duration of analgesic effectiveness than unbuffered aspirin. (CX 514 at 35378).

597. The FDA Panel placed Bufferin's "faster" claims in Category III. The Panel reached these conclusions after viewing voluminous submissions from Bristol-Myers, which included the same materials and arguments Bristol-Myers has raised in this proceeding (CX 506; Tr. 12115-16, 11443-45, 11469-70, 11630-31, 11640, 11644-47, 11649, 11651-58).

598. The AMA Drug Evaluations (2d ed. 1973) also corroborates those views:

> . . . It has been suggested that the analgesic effect of aspirin is related to blood levels of acetylsalicylate rather than salicylate; however, it has not been possible to correlate these blood levels with the degree of analgesia in man. (CX 512, p. 261.)

599. Dr. Beaver wrote to AMA's Dr. Lewis in connection with the AMA drug evaluations, "Bufferin does have a somewhat higher dissolution and absorption rate than plain aspirin, but results of controlled studies have not conclusively demonstrated that the use of these mixtures results in fact in onset of greater or longer analgesic effect or less gastric upset than plain aspirin. (Tr. 4239).

600. Dr. Lewis testified that, although there is some correlation between blood levels and analgesia in some situations, studies have not conclusively demonstrated that Bufferin has faster onset, greater or longer action or less stomach upset (Tr. 4254-56).

601. The *Medical Letter*'s July 5, 1974 issue entitled "Is All Aspirin Alike?" provides further corroboration of the above views. Regarding buffered aspirin tablets, it states in part:

> "It has never been established in patients with painful conditions . . . that there is a difference between buffered and unbuffered aspirin in time of onset of analgesia, duration or degree of relief of pain, or incidence of gastrointestinal distress. (CX 510A-B).

602. The FDA Analgesic Panel seems to be using the word "correlation" in terms of a mathematical, that is statistical, relationship between blood level and analgesic effect (Tr. 9038). The Panel states:

> While current studies have failed to show a direct one-to-one correlation between plasma levels of an analgesic drug and pharmacologic response, there is some evidence that a complex nonlinear relationship between these two variables undoubtedly does exist and involves non-linear complex functions and time lags. . . . There are known relationships between dose and plasma concentration (also nonlinear). It follows logically and mathematically that some expression does exist and recent advances in computer assisted pharmacokinetic modeling, analytical methodology and analgesic testing will probably allow elucidation of this function in the future. When an insensitive test does not show clear differences between two products it can only be said that present insensitive methods cannot determine a difference between the two. In the absence of other evidence, no means of validating claims are available. (CX 514, pp. 35480-81).

603. Dr. Beaver testified that due to technical difficulties there have been unsuccessful attempts to correlate actual clini-

cal effect with blood salicylate levels by simultaneous collation of blood samples and measurements of analgesia (Tr. 5957).

604. Blood level studies are quite sensitive and can pick up small differences in blood level (Tr. 9053-54).

605. In order for there to be pharmacological action, the active principles of the drug must reach the site of action and in order to do so, must first get into the blood (Tr. 9038-39).

606. Bufferin puts unhydrolyzed aspirin and salicylate at given levels into the bloodstream faster than aspirin and it is reasonable to suspect and unreasonable to preclude the possibility that the dosage form that got into the bloodstream sooner (Bufferin) will produce clinical effect sooner (Beaver, Tr. 5955), since once into the blood, there is no pharmacological or physiological difference between plain aspirin and the aspirin from Bufferin (Beaver, Tr. 6063).

607. Dr. Azarnoff does not doubt that before pain relief can occur, sufficient quantities of pain reliever (aspirin, the active principle in Bufferin or Excedrin) must reach the receptor site in a sufficient amount to trigger the onset of pain relief (Tr. 9203-04) and that in order for the active principle of a pain reliever to reach the receptor site it must get into the blood and reach the receptor site via the bloodstream (Tr. 9204).

608. A later appearance of active principles in the bloodstream suggests, but does not necessarily prove, later onset of pain relief (Azarnoff, Tr. 9205). Similarly, an earlier appearance of active principles in the bloodstream suggests, but does not necessarily prove, earlier onset of pain relief.

609. The NAS/NRC Panel agreed that the Bristol-Myers submission and the published literature made a very good case that Bufferin is absorbed to some degree more rapidly than plain aspirin tablets (Tr. 5947-48). Dr. Beaver, a member of the Panel, refused to accept Bufferin's claims of faster relief because of a lack of substantial evidence, by which he meant clinical evidence from controlled analgesic studies (Tr. 6043).

610. Dr. Moertel, a clinical pharmacologist, indicated that absorption, excretion, metabolism, and various other factors all play a role in the onset of pain relief vis-a-vis blood levels,

and that for this reason Bristol-Myers' argument cannot be accepted as a substitute for the ultimate test of clinical trial (Moertel, Tr. 5803-05). Dr. Azarnoff, the only expert in pharmacokinetics who testified in this proceeding, stated that no conclusions can be drawn from blood level studies regarding a buffered product's speed in relieving pain (Azarnoff, Tr. 9195). If one desires to show faster pain relief, one would have to conduct a therapeutic trial (*i.e.*, a clinical study) of the drugs in question (Azarnoff, Tr. 9195). Finally, Dr. Beaver, who was a member of the NAS/NRC Panel that evaluated certain faster onset claims for Bufferin, testified that *nothing* that has developed in the literature—over the course of time from his review article in 1965 and the NAS/NRC Panel's review in 1967 up until present—has changed his view that Bufferin's faster onset of relief claims lack substantial evidence (Beaver, Tr. 6042).

611. The FDA's regulations concerning the bioavailability and bioequivalence of prescription drugs (*Bioavailability and Bioequivalence-Requirement*, 42 Fed. Reg. 1624, *codified as* 21 C.F.R. § 320), do not support respondent's contention that Bufferin is therapeutically superior to plain aspirin.

612. The purposes of the FDA bioequivalence regulations are (a) to identify pharmaceutically equivalent drugs, or pharmaceutical alternatives, "that are intended to be used interchangeably for the same therapeutic effect and that are not bioequivalent drug products"; and (b) to establish a "bioequivalence requirement for these drug products" (21 C.F.R. § 320.50). Thus, pharmaceutically equivalent drugs (*i.e.*, drug products that contain identical amounts of identical active ingredients, see 21 C.F.R. § 320.1(c)) become a concern under the regulations only if they are *not* "bioequivalent drug products."

613. For purposes of the FDA bioequivalence regulations, Bufferin and any well-formulated aspirin are not only pharmaceutical equivalents, but also bioequivalent drug products. The regulations define "bioequivalent drug products" as pharmaceutical equivalents (or alternatives) "whose rate and extent of absorption [*i.e.*, bioavailability] do not show a sig-

nificant difference'' when administered at prescribed dosages. The regulations further note that:

> [s]ome pharmaceutical equivalents or pharmaceutical alternatives may be equivalent in the *extent* of their absorption but not in their rate of absorption and yet may be considered bioequivalent because such differences in the *rate* of absorption . . . are considered medically insignificant for the particular drug studied. 21 C.F.R. 320.1(e) (emphasis added).

614. Differences in *rate* of absorption become ''medically significant'' under the FDA regulations (and are therefore viewed as ''bioequivalence problems'') *only* if they ''would result in therapeutic failure or a hazard to the patient'' (42 Fed. Reg. at 1626). Only where such ''medically significant bioequivalence problems'' exist, will pharmaceutical equivalents (such as Bufferin and aspirin) be found ''not bioequivalent,'' for purposes of the FDA regulations (see generally, *Criteria and evidence to establish a bioequivalent requirement*, 21 C.F.R. § 320.52). In this proceeding, however, there is no suggestion that because of the difference in rate of absorption of Bufferin and correctly formulated plain aspirin, Bufferin may cause ''therapeutic failure or a hazard to the patient.''

615. The specific subpart of the FDA bioavailability regulations regarding intra- and inter-batch variation in bioavailability of a single drug product (21 C.F.R. § 320.21(f)(2)), cited by Dr. Lanman in his testimony (Lanman, Tr. 11663-71), are irrelevant to the issue of Bufferin's alleged therapeutic superiority to aspirin. Reference to batch variability in both the bioavailability and the bioequivalence regulations is clearly concerned with assuring the adequacy of manufacture and quality control in drug production. For drugs that are *already subject* to a bioequivalence requirement, the bio-equivalence regulations state that:

> the ability of a manufacturer to make a satisfactory product consistently in four batches will generally assure

> FDA that the methods of manufacture and quality control are adequate . . . (21 C.F.R. § 320.55).

Under the separate bioavailability section of the regulations, FDA will insist on further reassurance of the adequacy of methods of manufacture and quality control in the form of new bioavailability studies, where

> there are data demonstrating significant intra-batch and batch to batch variability, e.g plus or minus 25 percent, in the bioavailability of the drug product (21 C.F.R. § 320.2(f)(2)).

There is no mention in this subsection that the 25% variability standard is meant to apply to comparisons between *different* products. Clearly, the "plus or minus 25 percent" reference in this subpart of the bioavailability regulations is a guideline for monitoring lapses in manufacturing and quality control of a drug product, not a standard for determining therapeutic equivalence or nonequivalence. Therefore, this clearly allows no inference, as suggested by Dr. Lanman (Tr. 11671), that a drug manufacturer which deliberately "varies" the bioavailability of its product by "plus 25 percent" is in any way superior to other members of its product class.

616. The FDA regulations themselves make clear that the bioavailability of a drug and its effectiveness are separate and distinct issues:

> It is not . . . the intent of a bio-availability study to demonstrate effectiveness. The purpose of a bioavailability study is to determine the rate and extent of absorption. If a drug product is not bioavailable, it cannot be regarded as effective. However, a determination that a drug product is bioavailable is not in itself a determination of effectiveness. The requirement of evidence of bioavailability is intended to supplement, no[t] replace, clinical evidence of effectiveness. 42 Fed. Reg. at 1640.

In fact, the FDA anticipated arguments such as what Bristol-Myers has advocated in this proceeding and specifically warned that:

> The bioequivalence regulations are not an attempt to equate evidence of bioequivalence with evidence of relative therapeutic effectiveness . . . 42 Fed. Reg. at 1625.

617. Dr. Lanman further suggested that the FDA's willingness to accept *in vitro* testing or forms of *in vivo* testing other than clinical testing (in connection with the bioavailability and bioequivalence regulations) in some way indicated FDA's willingness to accept nonclinical, *in vitro* tests where the effectiveness of a class of drugs (*e.g.*, aspirin-based OTC drugs) has been demonstrated (Lanham, Tr. 11672-76). However, FDA's statement cited by Dr. Lanman relates to determination of bioavailability or bioequivalence, not comparative effectiveness. (42 Fed. Reg. at 1639, 1640). Since clinical tests are not designed to measure the rate and extent of drug absorption, FDA prefers that a more direct "accurate sensitive [and] reproducible" means of measurement be used where the issue relates to bioavailability, and not to the clinical effects of drugs on patients. (42 Fed. Reg. at 1640.) The FDA stated in requiring bioavailability data in New Drug Applications (in addition to evidence of effectiveness through clinical trials) that such data is "needed to assure that the dosage formulation intended for marketing has the same characteristics as the dosage formulation used in clinical trials to determine safety and effectiveness and that there is batch to batch consistency." 42 Fed. Reg. at 1639. Thus, clinical tests and bioavailability tests perform different, though complementary, functions. Preference for verification of bioavailability using *in vitro* measures of bioavailability in no way suggests any relaxation of FDA's clear requirements that issues of safety and efficacy be determined in clinical trials (F. 516 *supra*).

618. It is concluded that the sole purpose of the FDA's bioavailability requirements is to ensure that different batches of an approved drug fabricated by an approved manufacturer or a chemically identical product fabricated by another manufacturer be bioequivalent to the original product which had been approved on the basis of well-controlled clinical studies. The rationale of the FDA bioavailability requirements is to de-

termine whether product A. delivers as much active moiety in the blood as the standard drug and is not applicable to the question in this proceeding of whether an earlier blood level of aspirin proves earlier onset of analgesia in clinical pain.

619. For the same reasons discussed hereinabove (F. 561-618 *supra*), it has not been established that Bufferin relieves pain *twice* as fast as aspirin (Complaint ¶ 7(B)(2)).

620. Bristol-Myers has represented that Bufferin relieves pain faster than aspirin for over 25 years. Throughout that period, it has never subjected that claim to clinical testing despite its realization of the importance of clinical studies to support its superiority claims for Excedrin and despite its public position that faster onset claims must be proved by clinical tests (F. 561, *supra*). In the face of evidence supplied by two respected panels of experts (CX 511 and CX 514), by publications relied upon by scientists in the field (CX 510, 512, 518), and by the testimony of four independent expert witnesses in this proceeding, it is found that it has not been scientifically established that the speed of relief provided by Bufferin is significantly greater than that provided by plain aspirin.

2. *Claims that Tests Prove Bufferin Is Twice As Fast*

621. Bristol-Myers represented that tests prove Bufferin acts twice as fast (F. 262-64 *supra*; Complaint ¶ 14A). These "tests" referred to in respondent's advertisements are "blood level" studies (CX 519C, D, 521, 522, 523-26, 527, 530, 788; Azarnoff, Tr. 9190-91; CX 536I (Spec 13a); CX 519A; Tr. 3861-71). Dr. Azarnoff specifically addressed these blood level studies, and the issue of whether they prove that Bufferin relieves pain twice as fast as aspirin. He stated that they are blood level studies that show only that buffered aspirin is somewhat more rapidly absorbed than unbuffered aspirin and that no conclusions regarding buffered aspirin's pain relieving speed can be drawn from them (Azarnoff, Tr. 9192-95). Therefore, it is found that Bristol-Myers' speed claim challenged in Paragraph 14A is false.

3. *The Substantial Question*

622. Because Bufferin's superior speed of action claims challenged in Complaint Paragraph 7(A)(1)-(3) have not been scientifically established according to the criteria set forth and adhered to by experts in the relevant scientific community, these claims were made in the face of a substantial question recognized by such experts as to their validity as alleged in Complaint Paragraph 9(A)(1)-(3) and 10.

E. It Has Not Been Scientifically Established That Bufferin Causes Significantly Less Stomach Upset Than Plain Aspirin

623. Bufferin contains 5 grains of aspirin, 97.2 mgs. of basic magnesium carbonate and 49 mgs. of dihydroxy aluminum aminoacetate (aluminum glycinate) (CX 925C, R; CX 927I).

624. Magnesium carbonate and dihydroxyaluminum aminoacetate (aluminum glycinate) are recognized antacids (CX 514, p. 35469). An antacid may be defined as "[a]n agent that reacts with acid, such as the hydrochloric acid of the stomach (gastric acid), to neutralize it (decrease its amount)" (CX 514, p. 35373).

625. While it has been suggested by some that the presence of antacids of the type and in the amount found in Bufferin may lessen gastric irritation by speeding the dissolution of the aspirin tablet, and thereby increasing the rate at which aspirin leaves the stomach and is absorbed into the system, this theory is open to serious doubt (Grossman, Tr. 7772; CX 518G; CX 512H). To the extent the antacids in Bufferin increase aspirin dissolution, the increase is quite small (Grossman, Tr. 7772). The best that can arguably be claimed on the basis of biomedical evidence is that, for the relatively small population subset who experience occasional gastric discomfort from aspirin ingestion, Bufferin may reasonably be expected to provide somewhat less gastric discomfort for some of them some of the time.

626. The FDA OTC Internal Analgesics Panel has noted

that "there is little meaningful difference between the rates of absorption of sodium salicylate, aspirin and the numerous buffered aspirin preparations of salicylates" (CX 514, p. 35378).

627. It is generally agreed that disintegration rate is the limiting factor for absorption. While it is known that buffers can speed up disintegration of an aspirin tablet, the disintegration rate of an aspirin product such as Bufferin depends on many other factors. The disintegration and dissolution rate of aspirin is probably as dependent on the way it is made as the addition of buffers (Grossman, Tr. 7772), as well as the amount of food in the stomach (CX 514, p. 35378).

628. However, even if the increased rate of dissolution, disintegration and absorption of aspirin is appreciably increased by the addition of antacids, there is not direct evidence to date linking this phenomenon with a decrease in aspirin side effects such as stomach distress (Grossman, Tr. 7772).

629. Nor could antacids in the amount present in Bufferin be expected to neutralize the acidity of the stomach's contents and thereby lower the incidence of stomach distress associated with aspirin (Grossman, Tr. 7772, 7786-89, 7800). The amount of antacid in Bufferin is barely sufficient to neutralize the acid present in the aspirin portion of Bufferin and could not significantly decrease, much less neutralize, the acidity of the stomach's contents as a whole (Grossman, Tr. 7771-72). Therefore, Bufferin could not decrease the damaging effects of aspirin on the stomach because it cannot neutralize the acid in it (Grossman, Tr. 7800). While respondent suggested that Bufferin was formulated as a substitute for the simultaneous administration of antacid with aspirin (Lanman, Tr. 11472-73), an effective dose of antacid employed for this purpose has over 75 times as much neutralizing capacity as Bufferin (Grossman, Tr. 7774).

630. Furthermore, since the addition of antacids to aspirin would only have effects prior to the absorption of aspirin into the system, it could in no event decrease the *systemic* effects of aspirin, which may contribute to aspirin-related stomach distress (Grossman, Tr. 7772-73; F. 651 *infra*).

631. Bristol-Myers did not present the testimony of a single expert witness in the field of gastroenterology. Again, its Medical Director, Dr. Lanman, offered the only testimony supporting its position. Dr. Lanman has no experience of any kind in this field of science (BMRX 1). On the other hand, complaint counsel offered Dr. Morton Grossman, a renowned gastroenterologist (F. 44-47, *supra*), well qualified to render expert testimony on Bufferin's claims relating to side effects and on the issue of the medically significant side effects of aspirin.

632. The FDA OTC Analgesics Panel placed the claim that buffered aspirin "may prevent the stomach distress that plain aspirin occasionally causes . . ." in Category III finding available data insufficient to support the claim (CX 514, p. 35480). The Panel further noted that, even if buffered aspirin does reduce the incidence of aspirin-associated stomach distress, it would do so in "some but not all patients who exhibit gastric intolerance with plain aspirin tablets," and that the number of persons who might benefit from buffered aspirin over plain aspirin "is probably small," (CX 514, p. 35470). The Panel urged individual evaluation of label claims for buffered aspirin's lower incidence of gastric intolerance out of concern that such claims not "imply . . . decreased incidence of gastric distress is significant for most people" (CX 514, p. 35470). Moreover, the Panel stated: "Based upon the total evidence available to the Panel, it concludes that the evidence is insufficient to substantiate the claims that buffered aspirin or highly buffered aspirin solution is safe for use in patients who should not take regular, unbuffered (plain) aspirin" (CX 514, p. 35471). Dr. Grossman testified he would never prescribe Bufferin to a patient who experiences gastric intolerance with aspirin but would instead prescribe a non-aspirin, *e.g.*, acetaminophe, product; if, as in rheumatoid arthritis, the patient were required to take aspirin, Dr. Grossman would place the patient on a full antacid regimen to be simultaneously administered with aspirin (Grossman, Tr. 7773).

633. There are no well-controlled clinical studies demon-

strating that buffered aspirin, such as Bufferin, causes stomach distress less frequently than plain aspirin (Grossman, Tr. 7769-70; F. 634-42 *infra*). The existing evidence is equivocal at best (Grossman, Tr. 7770). The NAS/NRC Panel (CX 511) reviewed the claim that Bufferin helps prevent stomach upset often caused by aspirin, and concluded that most of the published studies with which it was familiar indicated little difference in the incidence or intensity of side effects from Bufferin or plain aspirin (CX 511F). The *Medical Letter* (CX 510) concluded that it has never been established that there is a difference between buffered and nonbuffered aspirin, *inter alia*, as regards incidence of gastrointestinal distress (CX 510B). Two editions of the *AMA Drug Evaluation* (CX 512, CX 518) similarly concluded that controlled clinical studies have not conclusively demonstrated that buffered aspirin will result, *inter alia*, in less gastric upset than plain aspirin (CX 518G; CX 512H). The FDA OTC Analgesics Panel placed the claim that buffered aspirin "may" cause less incidence of gastric intolerance in Category III, available evidence being insufficient to support the claim (F. 632, *supra*).

634. Respondent cited four (4) clinical studies which purported to compare the incidence of side effects with plain aspirin and Bufferin and reported a lower incidence of stomach upset with Bufferin. However none of these studies were "well-controlled." (F. 635-40, *infra*).

635. In the first study, by Tebrock, subjects who reported to a number of industrial clinics with ailments for which aspirin was normally prescribed were given Bufferin, and they were later interrogated regarding side effects (Lanman, Tr. 11478, 11486). The subjects were asked to compare the side effects they experienced in the study with their past experience with plain aspirin (Lanman, Tr. 11486). Such a "clinical" study is entitled too little weight in this proceeding. The subjects in this study were not tested with aspirin on a blinded or any other basis (Lanman, Tr. 12047). The study called for no administration of an aspirin treatment. The subjects reported the incidence of side effects with 12 tablets of Bufferin (2 tablets every 3 hours), while in the study, and then were asked to

compare this side effects experience with Bufferin with what they remembered about past stomach distress which they thought was associated with plain aspirin (Lanman, Tr. 11486). This is called an "historical control" (Lanman, Tr. 12047). There is no way to determine whether the test subjects here accurately remembered and recounted their past experience with aspirin side effects, or, more importantly, whether they were able to distinguish side effects attributable to aspirin from gastric discomfort occasioned by any one of a number of other possible causes (Lanman, Tr. 12043-44).

636. The design used in the Tebrock Study — employing a "historical control" — was described by Dr. Sunshine as "so far afield from reality" that he could not comment on its validity (Sunshine, Tr. 9686). The FDA regulations allow "historical controls" only where the nature and course of the disease being studied, if left untreated or treated by means other than the test treatment, is so well known and unacceptable that historical control is the only alternative to clinical trial, for example, the "high and predictable mortality" of childhood leukemia. *See* 21 C.F.R. §§ 314.111(a)(4).

637. For similar reasons, in the second study, by Paul (CX 786), cited by respondent (Lanman, Tr. 11486-88), does not even approximate a well-controlled clinical trial. Only Bufferin was tested in the trial, using "historical control." For these reasons, the Paul Study is not reliable.

638. The third study, by Fremont-Smith, was published in the *Journal of the American Medical Association* in 1955. The study employed subjects suffering from arthritis and was divided in two parts: one involving short-term and the other long-term crossover administration of Bufferin and aspirin (Lanman, Tr. 11489). The long-term portion of the study was an "open trial," *i.e.*, both subject and investigator knew which drug was being administered, and thus cannot qualify for consideration as a well-controlled clinical investigation (Grossman, Tr. 7962). Apparently, only the short-term part of the study was double-blind (Lanman, Tr. 11489). However, patients were not randomly assigned to treatments (Grossman, Tr. 7961): aspirin was given first to *most* subjects, then Buff-

erin (Lanman, Tr. 11489). The problem of drug administration "order effects" was thus built into the design of the study. The order in which test drugs are administered can significantly affect the results of a study unless controlled for, and a clinical study is seriously flawed if drugs are given in the same sequence to all subjects, and there is no way to examine the effects of such order bias (Sunshine, Tr. 9682, 9829). The physiological and psychological "carry over" problems which result where only one test drug is given during a particular period of the study (*e.g.*, here, where only aspirin was given for the first treatment), and/or the test drugs are given in the same order to all patients, can lead to very, very misleading results" (Laska, Tr. 10433). A more proper way to conduct a study comparing two drugs is to randomize the patients to the treatments, or simply to give half the subjects one drug (*e.g.*, Bufferin) and half the other (*e.g.*, plain aspirin) during each period of treatment in the study (Laska, Tr. 10435).

639. Another flaw in the Fremont-Smith study lies in the fact that while the nurse administering the drugs and recording subject reactions to them was blinded, there is no statement that the nurse was unaware when the changeover was made from aspirin to Bufferin (Lanman, Tr. 12052), seriously compromising the blinding design of the study. The study itself notes that arthritic patients were subject to a variety of gastrointestinal abnormalities (Lanman, Tr. 12050). Therefore, even if it were otherwise well-controlled, the study might be generalizable only to persons suffering similar gastrointestinal abnormalities (Lanman, Tr. 12050). Dr. Grossman noted that the report of the study, as published, did not provide sufficient information to allow full evaluation (Grossman, Tr. 7961). Dr. Grossman also noted that there have been no published studies since the 1955 Fremont-Smith Study which purport to be well-controlled and double blind, addressing the same question. If such studies had been done, they would be of great interest to the medical community and would have been published (Grossman, Tr. 8011).

640. The third study (1958), by a Dr. Sher (CX 506Z572-Z580), reported the results of a clinical trial conducted at a

prison hospital in Michigan, comparing the incidence of gastric intolerance with Bufferin, four (4) unnamed brands of aspirin, and three (3) unnamed APC products (Lanman, Tr. 11491-98). The Sher study is entitled to little weight in this proceeding. The study was never published (Lanman, Tr. 12061). Dr. Lanman, the only witness who testified about the study, was not even employed by Bristol-Myers at the time the study was undertaken (Lanman, Tr. 12054). While it is known that Dr. Sher was a prison doctor (Lanman, Tr. 12054), there is no evidence that he had ever conducted clinical research before this study (Lanman, Tr. 12054). Nor is there any evidence of the identity, qualifications, experience and training of others who administered the study. For all we know, they may have been prison "trusties" or other untrained personnel. Dr. Lanman admitted it was highly likely that Sher's study was submitted by Bristol-Myers to the NAS/NRC Panel (Lanman, Tr. 12061), which considered Bufferin's claim of lower incidence of stomach upset and concluded that the claim lacked support (F. 633 *supra*).

641. Finally, respondent cited Dr. Calabro, a doctor who conducted some studies for Bristol-Myers in the mid-1960's (Lanman, Tr. 12040-41), for a statement regarding lessened abdominal complaints with buffered aspirin than with plain aspirin (Lanman, Tr.11501). The only basis for Dr. Calabro's statement is a reference to an article by Brewer (Lanman, Tr. 12035), which in turn cited no support other than personal experience (Lanman, Tr. 12036). This is nothing more than anecdotal evidence.

642. In sum, of the four clinical studies cited by respondent, two did not directly compare Bufferin and aspirin; one was not randomized, failed to correct for order effects, and therefore is seriously flawed; and one was unpublished, and there is no record evidence to attest to its reliability or to accord it any weight. Not one of the studies cited by Bristol-Myers meets the criteria of well-controlled clinical studies necessary to establish that there is a lower incidence of gastric distress with Bufferin than with plain aspirin. It is not surprising that Bristol-Myers had clinical studies, other than those it chose to rely

upon, which failed to show any superiority of Bufferin over aspirin with regard to gastric discomfort (Lanman, Tr. !i499).

643. Therefore, the advertising representations challenged in Paragraphs 7(A)(4) and 7(A)(5) of the Complaint were made in the face of a substantial question recognized by experts as to their validity, as alleged in Complaint Paragraphs 9(A)(4) and (5) and l0 and, therefore are false.

F. The Fact that Bufferin, Excedrin, and Excedrin P.M. Contain Aspirin is Not Known to a Substantial Number of Consumers and is a Material Fact Which Should be Disclosed in Advertising

1. *Gastrointestinal Effects of Aspirin*

644. Bufferin, Excedrin and Excedrin P.M. contain aspirin (F. 2, *supra*).

645. Aspirin has well recognized adverse effects on the gastrointestinal tract. These side effects include dyspepsia and massive gastrointestinal bleeding (Grossman, Tr. 7724-28, 7741-43, 7821, 7985). Aspirin can also exacerbate and may even cause gastric ulcers in substantial numbers of people (Grossman, Tr. 7727, 7744-45). It is well known among experts that initiation or exacerbation of stomach ulcers, stomach irritation and intestinal inflammation occurs in a significant number of individuals who take aspirin (CX 514, p. 35390).

646. Aspirin-induced dyspepsia includes general gastric discomfort, pain, nausea, and what is commonly called heartburn, occurring in the upper abdominal region (Grossman, Tr. 7724-25; CX 514, p. 35387).

647. Dyspepsia due to aspirin is a common occurrence (Grossman, Tr. 7725). The estimated incidence of dyspepsia in persons taking smaller doses of aspirin (*e.g.*, single dosages), is up to l0% (Grossman, Tr. 7725; CX 514, 35387). However, the estimated incidence increases to between 20 and 30% among those taking larger doses over an extended period of time, such as arthritics (Grossman, Tr. 7725-26).

648. Everyone experiences some occult blood loss (*i.e.*, imperceptible loss of blood) from the gastrointestinal tract upon

ingestion of aspirin (Grossman, Tr. 7757). However, such occult bleeding has no clinical significance, except in those few individuals with higher than normal blood loss and a tendency toward anemia, where bleeding induced anemia may occur (Grossman, Tr. 7757). No association has been established between occult bleeding and clinically important side effects of aspirin, such as dyspepsia and massive gastrointestinal bleeding (Grossman, Tr. 7758). While highly buffered aspirin (*e.g.*, aspirin preparations, such as Alka-Seltzer, containing larger quantities of antacids and in which the aspirin is put in soluble form) has been shown to reduce the magnitude of occult blood loss due to aspirin, it has not been shown that this decrease is associated with a decrease, for example, in dyspeptic symptoms (Grossman, Tr. 7759-60). Thus, the possibility that a buffered aspirin tablet may reduce aspirin-associated occult bleeding to a relatively small degree does not suggest that it would reduce incidence of clinically important gastrointestinal side effects (Grossman, Tr. 8012). All forms of aspirin, buffered or unbuffered, pose a potential hazard as regards clinically important gastrointestinal events (Grossman, Tr. 8008-09).

649. The available data are not sufficient to demonstrate that buffered aspirins, such as Bufferin, cause a lower incidence of dyspepsia than plain aspirin.

650. Aspirin, even in single doses, causes damage to the gastric mucosa in the form of lesions, detectable by visual examination and/or on microscopic examination (Grossman, Tr. 7758-59).

651. While the means by which aspirin injures the gastric mucosa, and thus causes adverse effects on the gastrointestinal tract has not been established, at least two mechanisms are involved: (1) a topical action (Davenport effect) in which aspirin, as it is absorbed into the gastric mucosa, causes injury in the form of erosion, hemorrhaging and cell damage (seen as lesions on the mucosa); (2) a systemic effect, in which aspirin after entering the bloodstream interferes with the normal mechanisms protecting the gastric mucosa (Grossman, Tr. 7762-64). In Dr. Grossman's opinion, both these mechanisms

contribute to gastrointestinal blood loss (Grossman, Tr. 7764).

652. Aspirin can cause massive life-threatening gastrointestinal bleeding (Grossman, Tr. 7727-28, 7741-43). Associations between ingestion of single doses and massive blood loss have been reported (Grossman, Tr. 7743; CX 514, p. 35393). Dr. Grossman estimated that 5 to 10% of massive gastrointestinal blood loss is due to aspirin ingestion (Grossman, Tr. 7985). Clinically important gastrointestinal blood loss can lead to weakness and shock, usually requires hospitalization, and may require surgical intervention (Grossman, Tr. 7742; CX 514, p. 35391). Severe gastrointestinal blood loss is the most serious adverse side effect of aspirin on the gastrointestinal tract (Grossman, Tr. 7741; CX 514, p. 35391). The mortality risk is high (CX 514, p. 35391). There is between a 5 and 10% mortality rate from severe gastrointestinal bleeding (Grossman, Tr. 7741).

653. The incidence of massive bleeding is not insignificant. There is a recognized higher risk of severe gastrointestinal blood loss among persons with peptic ulcers, and those who have had prior experiences of gastrointestinal blood loss or dyspepsia and these persons should avoid aspirin (Grossman, Tr. 7764; CX 514, p. 35392).

654. Aspirin may not only present a grave risk to those persons with pre-existing gastric ulcers, by increasing gastrointestinal bleeding, but in large doses may actually cause gastric ulcers (Grossman, Tr. 7727; CX 514, p. 35390). There is evidence that aspirin may produce a specific kind of ulcer, not seen in its absence (Grossman, Tr. 7745-47, 7753-54; CX 514, p. 35390).

655. Gastric ulcers are a serious disease, causing significant morbidity, stomach perforation, obstruction of the flow of food from the stomach, peritonitis, and often requiring surgery on the stomach (Grossman, Tr. 7756).

656. By conservative estimate, most notably reported by Levy in his Boston Collaborative Group studies, aspirin ingestion results in 10 out of every 100,000 users developing a gastric ulcer, requiring hospitalization (Grossman, Tr. 7840; CX 514, p. 35391). The Levy Study also estimated that one-eighth

of all gastric ulcers were related to aspirin (CX 514, p. 35390), and Dr. Grossman testified that a history of aspirin ingestion is found in 20 to 30% of individuals with gastric ulcers (Tr. 7756).

657. Dr. Grossman is familiar and agreed with the report of the FDA OTC Internal Analgesics Panel as it related to the nature, incidence and severity of aspirin-related side effects (Grossman, Tr.7782). In this connection, the FDA Panel noted, *inter alia*, that in a recent survey, the adverse effects of aspirin on the gastrointestinal tract were the second most frequent drug-involved adverse effect that was serious enough to require hospitalization. Two out of every 1,000 hospital admissions were attributed to aspirin (CX 514, p. 35392, reporting on the results of a survey by the Boston Collaborative Drug Surveillance Program).

658. Aspirin also interferes with blood clotting, and should be avoided by persons with a history of blood coagulation defects, those receiving anticoagulant drugs, or those with severe anemia (CX 514, p. 35385).

659. The FDA Analgesics Panel has recommended that the following warning appear on all aspirin-containing products, regardless of formulation: "Caution: Do not take this product if you have stomach distress, ulcers or bleeding problems except under the advice or supervision of a physician" (CX 514, p. 35395).

2. *Allergic Side Effects of Aspirin*

660. Aspirin may also have respiratory and allergic side effects including severe and even life threatening attacks to those suffering asthma.

661. An asthmatic attack involves a spasm and resulting constriction of the bronchial tubes. Symptoms include shortness of breath, coughing, and in severe cases, hypoxia (*i.e.*, insufficient delivery of oxygen to red blood cells), shock and occasionally death within minutes of an attack (Stevenson, Tr. 1481; Farr, Tr. 2565-66, 2571-72; CX 514, p. 35398).

662. Ingestion of anywhere from 3 mg. to 650 mg. of aspirin can cause an asthmatic attack among susceptible members

of the asthmatic population (Stevenson, Tr. 1480). The severity of the aspirin-induced asthmatic attack depends on the degree of bronchial constriction prior to ingestion of the aspirin. If the bronchial tubes are already partly closed, the attack can be severe or even life threatening (Stevenson, Tr. 1489).

663. Combining aspirin with buffering ingredients, as in Bufferin, will not mitigate aspirin's asthmatic side effects (Farr, Tr. 2576; Stevenson, Tr. 1490-91). While the number of asthmatics in the population is uncertain, as is the number of asthmatics sensitive to aspirin, the incidence of persons susceptible to aspirin-induced asthmatic attacks is not insignificant. Dr. Stevenson cited a 1972 study by Davis concluding that 9 million persons were under care for asthma (Stevenson, Tr. 1494).

664. The Tecumseh Study, an epidemiological study of health problems of the residents of a Michigan town, is the best evidence available on the incidence of asthmatics in the general population, and reported that 6% of the townspeople had conditions previously diagnosed as asthma, and another 6% had medical histories consistent with asthma (Stevenson, Tr. 1494).

665. Dr. Stevenson's own study, which "challenged" asthmatic patients not known to be sensitive to aspirin with aspirin, led him to conservatively estimate that 10% of the asthmatic population is sensitive to aspirin (Stevenson, Tr. 1498). A study by Dr. Farr found 17.36% of asthmatics intolerant to aspirin, a figure he believed low because certain high risk subjects were excluded from the study (Farr, Tr. 2589-2605). The FDA Analgesics Panel estimated that between 6 to 20% of asthmatics are sensitive to aspirin (CX 514, p. 35397).

666. Aspirin may also cause dermal allergic reactions, particularly urticaria (hives) and angiodema (giant hives and swelling) (Stevenson, Tr. 1512; CX 514, p. 35398). Such reactions are not usually life threatening (Stevenson, Tr. 1511; CX 514, p. 35398) but urticaria may be serious if the lining of the stomach is involved and angiodema may be fatal if swelling takes place in the vocal chords, cutting off breathing (Stevenson, Tr. 1512).

666a. In some persons a few molecules of aspirin will cause a dermal reaction, in others a relationship between dose and severity has been seen (Stevenson, Tr. 1513). By contrast to asthmatic reactions, the incidence of dermal reactions is very small (Stevenson, Tr. 1464).

667. The overall incidence and severity of allergic reactions to aspirin is such that the American Academy of Allergy, a professional organization with a membership of some 2,200 allergists, adopted the following resolution in 1973:

> while recognizing that acetylsalicylic acid (aspirin) is a valuable drug, the American Academy of Allergy recommends that a formulation containing aspirin and advertisements promoting the formulation should clearly indicate that the preparation contains aspirin and that aspirin can be harmful to some persons.

In the same year, the American College of Allergists, another professional organization of allergists, passed a similar resolution (Farr, Tr. 2608-12).

668. The FDA OTC Internal Analgesics Panel stated its agreement with the Academy resolution (CX 514, p. 35398). The Panel has recommended that the following warning should appear on all products containing aspirin:

> This product contains aspirin. Do not take this product if you are allergic to aspirin or if you have asthma except under the advice and supervision of a physician. (CX 514, p. 35399).

669. Disclosure in advertising that Bufferin, Excedrin and Excedrin P.M. contain aspirin would be important to the substantial number of people who for sound medical reasons should avoid aspirin and may not be aware that these products contain aspirin (Grossman, Tr. 7765-67; Moertel, Tr. 5625-26). There are large numbers of people who should avoid aspirin and are so warned (Grossman, Tr. 7767; Moertel, Tr. 5625-26). Dr. Stevenson testified, for example, that he warns patients he identifies as aspirin sensitive to avoid aspirin, but most asthmatics do not know if they are aspirin sensitive or

not, and should avoid aspirin as a precaution (Stevenson, Tr. 1502). Immunologists generally warn asthmatics to avoid aspirin (Farr, Tr. 2601-2606).

670. However, many patients do not know that an OTC aspirin product which does not contain "aspirin" in its brand name, such as Bufferin and Excedrin, in fact contains aspirin. Because of this problem, some persons warned not to take aspirin will take it anyway (Stevenson, Tr. 1509; Moertel, Tr. 5625-26; Grossman, Tr. 7766-67, 7879-80).

671. The particular danger posed by aspirin unawareness was made clear, in Dr. Moertel's experience, when large numbers of his patients, whom he warned against aspirin-containing drugs, took aspirin products not knowing their aspirin content. This subsequently caused gastrointestinal bleeding and hospitalization (Moertel, Tr. 5625-26). Dr. Grossman also cited a specific example of a patient suffering from a peptic ulcer, who was warned not to take aspirin, but who developed upper gastric bleeding and later recounted that he had taken Excedrin (Grossman, Tr. 7880).

672. Disclosure of aspirin content on the product label alone is not a sufficient means of alerting persons who should avoid aspirin. In the experience of doctors testifying in this proceeding, patients generally do not read labels on medications carefully, if at all (Grossman, Tr. 7767; Moertel, Tr. 5%25-26).

673. A substantial number of consumers do not know, and have not known for a long time, that Bufferin and Excedrin contain aspirin. In a survey of consumers conducted by the Gallup organization in 1964 (CX 333), only 19% of a nationally projectable sample could name aspirin as an ingredient in Bufferin on an unaided basis; 74% of the sample could not name any ingredient in Bufferin (CX 333H). In that same study, when consumers were directly asked whether aspirin was an ingredient in Bufferin, only 46% answered affirmatively (Ross, Tr. 7463- 64; CX 333J).

674. In the Vanquish Study (CX 347-48), the predominant response among Bufferin users who were asked to state the number of ingredients in Bufferin was "Don't know" (61%) (Ross, Tr. 7464-66; CX 348Z041); only 41% of those who

stated Bufferin contained "more than one ingredient" were able to name aspirin as an ingredient in Bufferin (Ross, Tr. 7464-66; CX 348Z043). The predominant response among Excedrin users who were asked to state the number of ingredients in Excedrin was "Don't know" (56.8%) (Ross, Tr. 7465; CX 348Z041); 33% of those who stated that Excedrin contained "more than one ingredient" could name aspirin as an ingredient in Excedrin (Ross, Tr. 7465-67; CX 348Z043). Only 33.1% of Bufferin users and 25.8% of Excedrin users agreed that "all advertised brands rely chiefly on aspirin to relieve pain," which indicates a general lack of awareness of aspirin as an ingredient in both Bufferin and Excedrin (Ross, Tr. 7467-68; CX 348Z251).

675. In the 1967 and 1970 Oxtoby-Smith studies (CX 1058 and 1059), consumers showed a general lack of awareness of ingredients by the magnitude of their responses to the question "I have little idea of ingredients in the headache tablets I take." In 1967, approximately 62.3% of male and 46.2% of female Bufferin users agreed with that statement and approximately 61.3% of male and 47.9% of female Excedrin users agreed; in 1970, approximately 63% of male and 49.2% of female Bufferin users agreed with that statement and 59.9% of male and 57.9% of female Excedrin users agreed (Ross, Tr. 7474-75; CX 1058Z460; CX 1059Z179).

676. In the 1972 Pain Reliever Telephone Study (CX 314), only 23% of the consumers surveyed were able to name aspirin as an ingredient in Bufferin (Ross, Tr. 7470-71; CX 314Z006); 70% of the sample surveyed could not name any ingredients in Bufferin (CX 314Z007). For Excedrin, only 21% of the consumers surveyed were able to name aspirin as an ingredient in Excedrin (Ross, Tr. 7471-72; CX 314Z008). Seventy-seven percent of the sample surveyed could not name any ingredients in Excedrin (CX 314Z009).

677. Dr. Moertel conducted an informal survey of two samples of individuals with whom he came in contact in his duties at the Mayo Clinic in the recent past (Moertel, Tr. 5626; CX 810A-C). The first sample consisted of 100 patients and their family members who came to the cancer treatment center at

the Currie Pavillion at the Clinic (Moertel, Tr. 5626). The second sample consisted of 100 paramedical personnel who, although nonphysicians, had some responsibility in dealing with medicine and worked in a medical setting (Moertel, Tr. 5626-27). A short form questionnaire, developed by Dr. Moertel, was self-administered by each respondent with the nurse technicians at the clinic available to answer any questions regarding the form. The questionnaire included questions about age, sex, educational level and asked whether a number of drugs printed on the questionnaire contained aspirin. Respondents were simply asked to check "yes" or "no" or "don't know" (Moertel, Tr. 5626- 27; CX 810A).

678. Ninety percent of the paramedics correctly identified aspirin as an ingredient in Bufferin; 3% said Bufferin did not contain aspirin; and 7% checked the "don't know" response (Moertel, Tr. 5629; CX 810B). For Excedrin, 84% of the paramedics correctly identified aspirin as an ingredient in Excedrin; 1% stated Excedrin did not contain aspirin; and 15% checked the "don't know" response (Moertel, Tr. 5630; CX 810B).

679. Of the 100 patient/family member sample, 68% correctly indicated that Bufferin contained aspirin; 4% stated Bufferin did not contain aspirin; and 28% did not know. For Excedrin, 65% correctly indicated that Excedrin contained aspirin; 1% stated Excedrin did not contain aspirin; and 34% stated they did not know (Moertel, Tr. 5631; CX 810C).

680. Mr. Ivan Combe, the Chairman of the Council on Family Health ("CFH") (Tr. 9397), testified that CFH has been preparing and making available to networks, television stations, and magazines, advertisements advising consumers to read the labels of drug products since 1972 (Tr. 939H-17; 9401-02). BMRX 128 contains copies of five such film advertisements (Tr. 9404). BMRX 17A-E are copies of print advertisements which CFH supplied to magazines and newspapers for public service exposure (Tr. 9405-08).

681. The value of the television time allocated to CFH's read-the-label campaign in 1977 was approximately $2.7 million in 1976 and $500,000 in 1975. The value of the broadcast

time and print space for CFH's read-the-label campaign during 1974 was approximately $1.25 million (Tr. 9414-24). One print advertisement alone, "Why trust your memory when you can be sure," appeared in a number of major magazines, including Good Housekeeping, Esquire, Family Health, U.S. News & World Report, People and Business Week with an estimated exposure to 4.6 million people (Tr. 9453) (BMRX 17E).

682. The purpose of the read-the-label campaign is to inform the consumer on the proper use of medicines in the interest of safety and efficacy (Tr. 9440). CFH felt that the use of a succinct, incisive message would be most effective in communicating to consumers (Tr. 9442-43; 9448-49). The theory behind the campaign is that, if the public is given the right general advice and they follow it, all of the specifics will be covered (Tr. 9451) including awareness of the ingredients contained in the drug product (Tr. 9456).

683. It is found that the primary purpose of the "read the label campaign" is to educate the consumer to read and heed the label instructions regarding doses in the interest of safety and efficacy of OTC drug products. As such the campaign is important in view of the fact that many OTC drug products, such as analgesics, contain potent drugs and can cause serious harm when misused or abused. However it is highly doubtful whether the consumer who reads the label for dose information will also read the ingredients information.

684. Thus, the fact that Bufferin and Excedrin contain aspirin is a material fact and is not known to a substantial number of consumers. A failure to disclose that material fact in advertising for these products is misleading and deceptive. Therefore, the existence of aspirin in Bufferin and Excedrin should be disclosed in all advertising for these products.

G. The Ingredients, Either Individually Or In Combination, In Bufferin, Excedrin or Excedrin P.M. Do Not Relieve Tension

685. Tension (often used synonymously with "anxiety") exhibits symptoms such as headache, depression, anger, hos-

tility, fear, heart palpitation and perspiration (Rickels, Tr. 6516-17) and is appropriately treated with antianxiety agents or tranquilizers (Rickels, Tr. 6525; CX 513Z003).

686. From 1961-1970 Bristol-Myers made claims in advertisements that Bufferin, Excedrin and Excedrin P.M. will relieve tension, stress, anxiety and enable persons to cope with the ordinary stresses of everyday life. It also made claims of efficacy for tension relief in labels of Bufferin and Excedrin (CX 815; CX 816; CX 817; CX 818; CX 820; CX 800).

687. The nonantacid active ingredient in Bufferin is aspirin. The ingredients in Excedrin are acetaminophen, salicylamide, aspirin and caffeine. The ingredients in Excedrin P.M. are acetaminophen, salicylamide, aspirin and methapyrilene fumarate. None of these ingredients, either alone or in combination, are considered to be effective antianxiety agents or tension relievers. An ingredient in Excedrin — caffeine — is contraindicated for the treatment of tension.

688. Headache pain can be a symptom of tension. In such instances, the headache pain is caused by the underlying tension (Rickels, Tr. 6518, 6524). Underlying tension may also, however, exist simultaneously with, but independently of, a headache without causing it (Rickels, Tr. 6519-20). In such a case the headache is caused by something other than the underlying tension. In either case, however, this headache pain may act to aggravate underlying tension; *i.e.*, someone becomes tense, or more tense, because he has a headache. This situation is called the "tension-headache-tension" cycle (Rickels, Tr. 6519-20, 6524). In those instances when an individual is suffering from tension, which causes a headache as one of its symptoms, aspirin is neither appropriate nor indicated for the treatment of the underlying tension (Rickels, Tr. 6532-33). As an analgesic, aspirin will relieve the pain of headache and, because that pain is gone, the tension caused by the pain may be lessened. But the aspirin will never treat the tension that caused headache in the first place (Rickels, Tr. 6525-27, 6530). Therefore, the only sense in which aspirin can be considered a tension reliever is that it may indirectly relieve the tension caused wholly by pain while not affecting

the underlying tension (Rickels, Tr. 6528). To consider aspirin a tension reliever would be the same as calling an antibiotic a tension reliever in a situation where an infection causes one to be tense. The antibiotic relieves the infection which, in turn, would relieve the tension caused by having an infection. But neither aspirin nor the antibiotic can be said to be tension relievers because neither has any direct tension relieving properties; neither is helpful in treating tension *per se* (Rickels, Tr. 6528-29).

689. In determining whether there is reason to believe that a drug has tension relieving properties, information derived from a well-controlled, randomized double-blinded clinical study in a well-defined population is given the most weight (Rickels, Tr. 6499, 6529-30, 6548).

690. Dr. Lanman, Bristol-Myers' Medical Director, stated that Bristol-Myers relied on four published papers, an article, and a textbook as its basis for the claim that aspirin and acetaminophen have tension relieving properties. Specifically, the materials relied upon by Bristol-Myers are: (1) two studies by Krumholtz and Merlis, dated 1964 and 1965; (2) a 1954 medical textbook, *Pharmacology and Medicine*, edited by Drill; (3) a 1957 review article entitled "Current Concepts in Therapy" published in the New England Journal of Medicine; (4) a 1957 report by Boyd, Gittinger, and Schwimmer entitled "Sleep Induction With Salicylamide and Acetophenetidin"; and (5) a 1959 report by Boyd, Huppert, Sullivan, and Molinus entitled "Hypnotic Effects of Bufferin" (Lanman, Tr. 12161-74). Bristol-Myers has never funded a study to determine or evaluate the amount or degree of tension relief afforded by Bufferin, Excedrin or Excedrin P.M. (CX 925J; CX 927B).

691. All of the six sources relied upon by Bristol-Myers are dated. The Drill textbook is dated as early as 1954. Dr. Lanman was asked if Bristol-Myers could supply a more recent edition of this textbook which contains the same purported support, but Dr. Lanman stated that he could not (Lanman, Tr. 12169). The other sources are dated from 1957 to 1965. In 1965, a date when all materials relied upon by Bris-

tol-Myers in this proceeding were extant, Dr. Beaver completed a comprehensive review of all the sources of evidence — including those solicited directly from Bristol-Myers — on the pharmacologic properties of analgesics (Beaver, Tr. 5897-5900). He specifically found that among the over 1,000 articles and other materials he analyzed there was "no good evidence" that mild analgesics have tension relieving properties (Beaver, Tr. 5897-98; Lanman, Tr. 12151-54).

692. The two Krumholtz and Merlis studies, the only post-1959 studies cited by Dr. Lanman, while interesting, are not the sort of evidence which scientists in biomedicine generally accept as establishing a proposition. The studies used volunteers and apparently were not randomized (Rickels, Tr. 6572, 6579-80). The authors also do not use the standard index for the measurement of tension relief (Rickels, Tr. 6573-74). The authors reported insufficient data to allow a meaningful analysis of their results (Rickels, Tr. 6572, 6579). Above all the authors themselves recognized the deficiencies of their data, concluding that further studies were needed to test the efficacy of aspirin as a tension reliever (Rickels, Tr. 6634-35; Lanman, Tr. 12258). Likewise, Dr. Beaver, in his landmark review of literature on mild analgesics, explicitly referred to the Krumholtz and Merlis studies as not providing evidence of tension relieving properties of aspirin and merely "productive of inconsistent results" (Lanman, Tr. 12152).

693. The 1959 report by Boyd, Huppert, Sullivan, and Molinus does not provide a reasonable basis for the assertion that aspirin has tension relieving properties. The authors, whose reputations for research are not widely known, reported that Bufferin showed an ability to induce hypnotic (somnifacient) effects in the test subjects. However, it is not clear whether the sample of 102 custodial care patients (with a median age of 64) were randomized (Rickels, Tr. 6593). Apparently the authors used test subjects who had physical problems which produced pain. Therefore, it is possible that the reported results may be attributable to the pain relieving properties of aspirin rather than to any tension relieving properties of aspirin (Rickels, Tr. 6593). These methodological prob-

lems led Dr. Rickels to state that he had "great doubts about the results," particularly since they purport to show that Bufferin's tension relieving abilities exceeded those of most prescription drugs indicated for the relief of tension (Rickels, Tr. 6591-95).

694. The 1957 report by Boyd, Gittinger, and Schwimmer was on the hypnotic effects of a drug called Effisin, which contained salicylamide and acetophenetidin. Salicylamide is an ingredient in Excedrin. Dr. Lanman did not say that the ingredient salicylamide has any tension relieving properties. His position is limited to aspirin and acetaminophen (Lanman, Tr. 11509-10, 12149-51). In any event, Dr. Beaver, in his comprehensive review of all the research as of 1965 regarding the properties of mild analgesics (Beaver, Tr. 5897-99), found that there "was no good evidence" that such drugs had any tension relieving properties (Lanman, Tr. 12152).

695. The 1954 textbook by Drill and the 1957 review article published in the *New England Journal of Medicine* do not provide a reasonable basis to show the efficacy of aspirin or acetaminophen as tension relievers. Neither of them involved clinical trials. The FDA Panel on OTC Sedative, Tranquilizer and Sleep-Aid Drug Products did not consider such textbooks and review articles as evidence of a drug's efficacy in their evaluations (Rickels, Tr. 6547-48). Statements from the medical literature and textbooks relating to the tension relieving ability of analgesics were also not accorded much weight by Dr. Beaver in his comprehensive review of the scientific literature on this point. He found that the statements in the literature were often based on a study of three subjects (who were also the investigators) without the benefit of blinding or placebo controls (Lanman, Tr. 12154).

696. On the other hand, all authoritative studies published after Dr. Beaver's 1965 review article have consistently found that there was no evidence to show that mild OTC analgesics such as aspirin have tension relieving properties. Bristol-Myers continued to make tension relief claims for Bufferin, Excedrin, and Excedrin P.M. until 1970.

697. In a 1973 well-controlled, double-blinded clinical

study of Compoz, Librium, aspirin and placebo in normal doses in patients suffering moderate degrees of tension, aspirin was found not to be significantly different from placebo in terms of its ability to relieve tension (Rickels, Tr. 6500, 6511-13, 6517). This result is consistent with the creditable scientific literature regarding the lack of tension relieving properties of aspirin, and confirms Dr. Beaver's conclusion in 1965 that a therapeutic dose of aspirin cannot be considered a tension reliever (Rickels, Tr. 6517).

698. Further confirmation of this view is found in the FDA Internal Analgesic Panel, which concluded that aspirin is "clearly ineffective" for "nervous tension" (CX 514, p. 35355). Likewise, the FDA Advisory Panel on OTC Sedative, Tranquilizer, and Sleep-Aid Drug Products determined that aspirin was "ineffective" as a "daytime sedative" product, which the Panel defined as one that claims "mood-modifying indications such as for the relief of occasional simple nervous tension" (CX 513E, Z002; Rickels, Tr. 6538-39). The Sedative Panel made the same conclusions with respect to acetaminophen and salicylamide (CX 513E; Rickels, Tr. 6540).

699. In 1975, a minority of the FDA Sedative Panel considered methapyrilene (an ingredient in Excedrin P.M.) to be ineffective as a daytime sedative; *i.e.*, a tension reliever. A majority voted to place methapyrilene in Category III, that is to allow manufacturers limited time to develop studies to show the efficacy of methapyrilene as a daytime sedative (Rickels, Tr. 6541-42). While the majority recognized that the research at that time did not show any tension relieving properties for methapyrilene, they felt that the industry should be given an opportunity to identify any population which could benefit from that compound (Rickels, Tr. 6550-51). However, the unanimous opinion of the Panel was that the studies would never show methapyrilene's efficacy for the relief of nervous tension (Rickels, Tr. 6541, 6551). Since no research on this issue has been forthcoming, Dr. Rickels testified that all members of the Panel now believe that methapyrilene should be

placed in Category II as a daytime sedative (Rickels, Tr. 6541, 6550).

700. In 1972, after a review of the published literature and after having considered scientific materials submitted by Bristol-Myers in support of its labeling claims, the National Academy of Sciences-National Research Council (NAS/NRC) Drug Efficacy Study Group specifically considered the claim on Bufferin's label that it was indicated for "mild temporary tension" (CX 5IIC, F). The Panel found that while Bufferin was "possibly" effective for the relief of tension, there was "very little evidence that aspirin has any tranquilizing or sedative effect" (CX 5IIF).

701. The combination of antacids with the aspirin in Bufferin does not change aspirin's inability to relieve nervous tension. Thus Bufferin is not effective for the treatment of nervous tension (Rickels, Tr. 6534).

702. The ingredients in Excedrin (aspirin, salicylamide, acetaminophen and caffeine) either alone or in combination are not effective for the relief of nervous tension (Rickels, Tr. 6532). In fact, the recommended dose of Excedrin contains 130 mg. of caffeine, a dose in excess of the clinical dose of caffeine (100 mg.) prescribed as stimulant (Rickels, Tr. 6530-31). A daily dosage of 8 Excedrin tablets contains 520 milligrams of caffeine which is just short of the level of 600-650 milligrams of caffeine which are known to cause anxiety (Rickels, Tr. 6530-31). The tension reliever claim for Excedrin is patently inconsistent with the presence of such a high level of caffeine in Excedrin.

703. The principal difference between Excedrin and Excedrin P.M. is that Excedrin P.M., in addition to aspirin, acetaminophen and salicylamide, contains methapyrilene instead of caffeine (Rickels, Tr. 6541; F. 2 *supra*). The substitution of methapyrilene for caffeine, a stimulant, does not make Excedrin P.M. effective for the relief of nervous tension. The three ingredients Excedrin P.M. shares with Excedrin are not effective for tension relief. The addition of methapyrilene, an ineffective drug for the relief of nervous tension (F. 699, *supra*), will not alter that result. Thus Excedrin P.M. is not

effective for the relief of nervous tension.

704. Respondent Bristol-Myers did not have a reasonable basis for the claims that Bufferin, Excedrin and Excedrin P.M. relieve nervous tension (Rickels, Tr. 6530; F. 691-700, *supra*). None of the materials offered by Bristol-Myers are sufficient to substantiate such claims. The four research studies offered by respondent all had serious methodological defects and cannot be considered to be well-controlled clinical studies. The other sources offered by respondent were statements found in dated and superseded scientific literature, and thus cannot be accorded much, if any, weight. The inadequacy of these sources is confirmed by Dr. Beaver's comprehensive published review in 1965 of all the sources on this issue which explicitly dismissed the only current evidence relied on by Bristol-Myers and which found that there was no good evidence that mild analgesics have any tension relieving properties. The inadequacy of Bristol-Myers' sources has also been confirmed by three panels of independent scientific experts: the FDA Internal Analgesic Panel, the FDA Sedative Panel, and the NAS/NRC Drug Efficacy Study Group, all of which found that there was insufficient evidence to support a claim that aspirin has tension relieving properties. It was also the testimony of one of the country's foremost experts in psychopharmacology, Dr. Rickels, that the available scientific evidence does not support any tension relieving claim for mild analgesics. Thus the record clearly shows that during the time respondent disseminated tension relief claims, there was no reasonable basis for the claim that its mild OTC analgesics had tension relieving properties.

H. Other Representations for Bufferin and Excedrin P.M.

1. *The "Doctors Recommended" Claim for Bufferin Lacked a Reasonable Basis*

705. Particularly through use of the phrase "Doctors specify Bufferin for minor pain more than any leading brand of pain reliever you can buy," respondents represented that

physicians recommend Bufferin more than any other nonprescription analgesic (Complaint ¶ 17; F. 253, *supra*). This representation was unfair and deceptive because respondents did not possess or rely on competent and reliable evidence sufficient to provide a reasonable basis for it.

706. In substantiation for this claim, Bristol-Myers submitted to complaint counsel, in response to subpoena, documents received in evidence as CX 364-390 and 676 (CX 838A). CX 364-380 comprise 17 portions of the National Prescription Audit (NPA), a national survey of drug prescription activity (CX 838A). CX 381-390 are portions of the National Disease and Therapeutic Index (NDTI), a national survey of drug treatment activity (CX 848E). CX 676 is explanatory material relating to the NPA (CX 838E). Neither the NPA nor the NDTI provide competent and reliable evidence in support of respondent's claim because: (a) the NPA monitors drug *prescription* activity and is not representative of doctors' recommendations for the *nonprescription* drugs that are in issue here; (b) the NDTI, which unlike the NPA is designed to reflect doctors' recommendations of both nonprescription and prescription drugs, shows doctors recommending other nonprescription analgesics more than Bufferin (F. 708, *infra*).

707. NPA is a continuing measure of the flow of drugs from retail pharmacies to consumers via written or telephoned prescriptions. Thus, the basic data underlying the survey are physicians' formal presriptions (CX 838A, B).

708. The NDTI, unlike the NPA, is designed to measure the variety of ways a doctor might "recommend" a nonprescription, internal analgesic. It includes prescription activity, but also includes, *inter alia*, drug issuance by the physician in a hospital, and drug recommendations made by the physician but not formally prescribed (CX 838G). Furthermore, a doctors' recommendations and issuance activity are categorized in NDTI reports in terms of "desired actions" (*e.g.*, "pain relief," "antiarthritic") allowing a more specific determination of whether doctors recommend Bufferin most for relief of "minor pain" (CX 838H-I; Complaint ¶ 17; Ross, Tr. 7378-79). The data for the period covered by the

submitted portions of NDTI (October 1967 through June 1971) support the following conclusions:

(a) First, construing "doctors' recommendations" broadly, to include all drug issuance activity by doctors *without* regard to the purposes for which the drugs were issued; as projected by NDTI, the total number of times Tylenol was recommended by doctors far exceeds the total number of times Bufferin was recommended. For example, according to the NDTI projection for the period July 1970 to June 1971, Bufferin was issued a total of 758,000 times while Tylenol was issued 1,774,000 times. (Ross, Tr. 7380-81; CX 822Z).

(b) Second, construing "doctors' recommendations" more narrowly and focusing on the issuance activity by doctors for "desired actions" relating solely to pain relief (the combined categories of "pain relief," "analgesic," "analgesic and pain relief," and "relieve headache"/"relieve headache and antipyretic"), the number of times doctors recommended Tylenol again far exceeds Bufferin, as does the number of times doctors recommended Ascriptin or generic aspirin (Ross, Tr. 7381; CX 822Z). For example, for the period July, 1970 to June, 1971, Bufferin was issued 404,000 times for these pain-related "desired actions," while issuances totalled 1,030,000 for Tylenol; 655,000 for Ascriptin; and 5,436,000 for generic aspirin (Ross, Tr. 7381; CX 822Z).

(c) Third, for each individual "desired action" relating to pain ("pain relief," "analgesic," or "relieve headache/antipyretic"), Tylenol issuances exceeded Bufferin issuances, as did issuances for generic aspirin (Ross, Tr. 7381; CX 822Y).

709. By any reasonable analysis of the 1971 NDTI, Tylenol and generic aspirin, and often Ascriptin, were "recommended" more often than Bufferin, and thus the claim alleged in Paragraph 17 could not reasonably be based on the NDTI data (Ross, Tr. 7382; CX 822Y, Z).

710. For reasons discussed hereinabove (F. 706-09, *supra*), respondents did not have a reasonable basis for the representation that physicians recommend Bufferin more than any other nonprescription internal analgesic at the time such claims were made (Complaint ¶ 18).

2. *Superiority Claims for Excedrin P.M.*

711. Respondents represented that it has been established that Excedrin P.M. relieves more pain than aspirin; that it is more effective for nighttime pain than aspirin; and that it is more effective than aspirin because it contains three ingredients (F. 357, *supra*).

712. Bristol-Myers has not sponsored or funded any studies in which subjects with slight to severe pain ingested Excedrin P.M. and which (1) compared the analgesic effects of Excedrin P.M. to the analgesic effects of aspirin; or which (2) compared the sedative, hypnotic or somnifacient effects of Excedrin P.M. to aspirin; or which (3) determined or evaluated the amount or degree of analgesic effects upon subjects who ingested Excedrin P.M. (CX 925J; CX 927H; CX 929D).

713. In order to establish the comparative efficacy of analgesics, well-controlled clinical tests are prerequisite (F. 364-94, *supra*). Bristol-Myers did not generate the only type and quality of evidence which could establish its claims relating to Excedrin P.M.'s superiority. Given that well-controlled clinical studies comparing Excedrin P.M. to aspirin do not exist, it has not been established that Excedrin P.M. is superior to aspirin, as alleged in Complaint Paragraphs 7B(9), (10) and 8.

714. Respondent has also represented that Excedrin P.M. contains a special ingredient, unique to its formulation (Complaint ¶ 23). In fact, the special ingredient is methapyrilene fumarate, an antihistamine available in other OTC medications such as Cope (Complaint ¶ 24; Answer of Bristol-Myers, Paragraph 1). By its admission that methapyrilene is available in other preparations besides Excedrin P.M., Bristol-Myers admitted that the uniqueness representation challenged in Paragraph 23 was false.

3. *Claims Concerning the Ingredients in Bufferin and Excedrin*

715. Respondent represented that the analgesic ingredient in Bufferin is other than ordinary aspirin (Complaint ¶ 21; F. 258, *supra*) when, in fact, aspirin is the only analgesic ingredient in Bufferin. Therefore, this representation was false (Complaint ¶ 22).

716. Respondent represented that the ingredient giving "long lasting relief" in certain Excedrin advertisements is something other than aspirin and the "antidepressant" is something other than caffeine (Complaint ¶ 21; F. 258, *supra*) when, in fact, the "long lasting relief" ingredient is aspirin (Lanman, Tr. 12150-51) and the "antidepressant" is caffeine (Lanman, Tr. 12150). Therefore, these representations were false (Complaint ¶ 22).

4. *Substantial Question*

717. Because the superiority claims for Excedrin P.M. have not been scientifically established, as alleged in Complaint Paragraph 7B(9)-(10), according to criteria accepted by experts in the relevant scientific community, those claims were made in the presence of a substantial question among such experts as to their validity, as alleged in Complaint Paragraphs 9B(9)-(10) and 10.

VI. Consumer Images of Bufferin and Excedrin

A. Introduction

718. From common sense and daily experience, the Bufferin and Excedrin advertising claims discussed in the preceeding sections and repeated during a long period of time, can reasonably be expected to create and maintain a product image or belief in the consumer's mind reflecting the advertising claims. The various surveys conducted by or for Bristol-Myers and other leading manufacturers of OTC analgesics confirm that conclusion.

719. An advertising penetration study is a survey which assesses the consumer's awareness of advertising claims dis-

seminated and the extent to which these advertising themes have penetrated and remained in the consumer's mind. Unlike copy tests, which focus attention on consumer's short-term recall of advertisements to which they have been exposed, usually within 24 hours, penetration studies have a much longer time reference; they measure consumers' recall of both the fact of advertising and its content over a period of time that generally exceeds several months (Ross, Tr. 7159-60). The "fact" of advertising refers solely to having seen any advertising for the brand. The "content" refers to the substance or specific themes of that advertising. Methods employed in penetration studies are similar to copy tests in that they both generally pose open-ended questions to the respondents with respect to their recall of the fact and the content of the advertising. This open-ended questioning calls for top-of-mind recollection of the advertising; *i.e.*, independent recall about the advertising with no probing for specific content by the interviewer. Consequently, penetration studies represent a lower bound estimate of the nature and amount of consumer's recall of advertising claims and themes (Ross, Tr. 7161). If a structured, closed-ended question were put to respondents testing the presence or absence of recall of a particular theme or content in an ad, the percentage of recall would be substantially higher (Ross, Tr. 7161). Also, since penetration studies reflect a longer period of time than copy tests, there is obviously a greater lapse between the time the consumer is exposed to the advertisements and the time the consumer is asked to recall them; accordingly, one reasonably would expect the level of response to be lower in the penetration study than in the copy tests (Ross, Tr. 7161).

B. Consumer Recall of Product Claims

720. Four advertising penetration studies in evidence, CX 310, CX 347, CX 326 and CX 345, contain questions relating to levels of both Bufferin and Excedrin advertising penetration in 1969, 1970, 1971 and 1973. The surveys first asked respondents whether they recalled any advertising for Bufferin and Excedrin (F. 723, *infra*; Tables I, II), and then whether they

recalled any specific claims being made for the product (F. 724, *infra*, Tables III, IV). These open-ended questions are lower estimates of recall of the advertising, and do not reflect the maximum number of people who had recall of specific claims. Despite the conservatism in the data produced by open-ended questions the results of these penetration studies demonstrate that (1) a substantial number of consumers remembered that Bufferin's advertising contained comparative speed and gentleness claims; and (2) a substantial number of consumers remembered that Excedrin's advertising contained comparative superiority claims and tension relieving claims (Ross, Tr. 7163; F. 724, *infra*).

721. Evidence from CX 310, *The 1969 Excedrin Study*, commissioned by Bristol-Myers, confirms that Bufferin's and Excedrin's comparative speed claims were remembered by consumers. This study is the only one of the four penetration studies that contained a closed-ended, or aided, recall question; its results show that consumers accurately remembered the advertising for the brands (Ross, Tr. 7178, 7198). For Bufferin, the study demonstrates that 39% of the total sample associated the claim "Goes to work in half the time" with Bufferin (Ross, Tr. 7178; CX 310Z095). With respect to Excedrin, 57% of the total sample correctly associated the claim "extra-strength pain reliever," and 44% associated the claim "For Headache No. 1040" with Excedrin (Ross, Tr. 7198-99). Consumers' distinctive and accurate attributions of these claims to Bufferin and Excedrin coupled with consumers' correct attributions of other claims to other competing brands demonstrates that consumers' answers to questions about what advertising they recall are not random commingling of claims for different products (Ross, Tr. 7178). Rather, consumers are demonstrating that they can correctly recall advertising for the brand about which they are thinking and that they associate the central claims made for Bufferin or Excedrin with each brand (Ross, Tr. 7178, 7198). The magnitude of correct responses to this closed-ended question supports the view that the generally lower percentage responses associated with open-end-penetration questions are

underestimates of the actual registration of advertising in the minds of the public (Ross, Tr. 7161).

722. A meaningful analysis of penetration data to reflect the content of recall should be limited to those consumers who said they recalled advertising for the brand (Ross, Tr. 7171). Percentage of content recall based on the total sample would include those who remembered no advertising for the product at all (Ross, Tr. 7171). Accordingly, whenever a study presented recall data percentaged against the entire sample, Dr. Ross adjusted that percentage by limiting its base to those who recalled the fact of advertising. Through simple division, Dr. Ross produced the relevant figures for recall of Bufferin and Excedrin advertising themes which appear in Tables III and IV, *infra* (Ross, Tr. 7171).

723. The results from the four studies in Table I (Bufferin) and Table II (Excedrin) demonstrate that over a four-year period from 1969 to 1973 between 36.8% and 43% of the samples recalled seeing some Bufferin advertising (Ross, Tr. 7170, 7182, 7187, 7192-7193); and between 36.6% and 66% of the samples recalled seeing some Excedrin advertising (Ross, Tr. 7196, 7200-01, 7202, 7204).

Table I

Percent Of Total Respondents Who Recalled Any Advertising For Bufferin

1969[1]	1970[2]	1971[3]	1973[4]
43%	39.9%	37%	36.8%

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[1] *CX-310 Z-090*, Z-146; Ross, Tr. 7169-7170.
"What do you recall being said in any advertising [during the past six months] for Bufferin?" "What was the main idea that the advertiser was trying to get across?"

[2] *CX-348 Z*; CX-347 Z-121; Ross, Tr. 7182-7185.
"Do you recall seeing or hearing any advertising for Bufferin in the past four weeks?"

[3] *CX-3260.C*; CX-1009A; Ross, Tr. 7186-7187.
"What does any advertising you have recently seen or heard say about Bufferin?"

[4] *CX-345 Z-027,-031,-033*, -107; Ross, Tr. 7191-7193.
"Have you seen or heard any recent advertising for any headache remedies or pain relievers?" "For which products or brands?" "Do you remember hearing or seeing any recent advertising for Bufferin?"

Table II

Percent Of Total Respondents Who Recalled Any Advertising For Excedrin

1969[1]	1970[2]	1971[3]	1973[4]
66%	48.8%	44%	36.6%

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[1] *CX-310 Z-090*, Z-146; Ross, Tr. 7196.
"What do you recall being said in any advertising [during the past six months] for Excedrin?" "What was the main idea that the advertiser was trying to get across?"

[2] *CX-348 S*; CX-347 Z-121; Ross,Tr. 7200-7201.
"Do you recall seeing or hearing any advertising for Excedrin in the past four weeks?"

[3] *CX-326 Z, C*; Ross, Tr. 7202.
"What does any advertising you have recently seen or heard say about Excedrin?"

[4] *CX-345 Z-027,-031,-033* -107; Ross, Tr. 7204.
"Have you seen or heard any recent advertising for any headache remedies or pain relievers?" "For which products or brands?" "Do you remember hearing or seeing any recent advertising for Excedrin?"

724. Tables III and IV detail the portion of consumers who remembered comparative speed and gentleness claims in Bufferin advertising, and comparative speed, strength and effectiveness claims in Excedrin advertising, respectively. The data in Tables III and IV are derived from the three studies which inquired into the content of recall, and they are appropriately percentaged against the more meaningful bases of those respondents who recalled Bufferin's or Excedrin's advertising (Ross, Tr. 7171). In examining the extent to which these consumers remembered superior efficacy claims for Excedrin, recall of strength and effectiveness claims should be assessed as aspects of comparative superiority in pain relieving efficacy (Ross, Tr. 7196-98, 7202-03, 7204-05; F. 736, *infra*).

725. In assessing the magnitude of the top-of-mind, completely unaided speed and gentleness recall for Bufferin, and superior efficacy recall for Excedrin, the absolute size of the percentages is not nearly as important as their size relative to the recall of other types of claims (Ross, Tr. 7315-16; 7329; 7330; 7444-46; 7450-51). Significantly more consumers recalled comparative claims than recalled the simple fact that the product was a pain reliever or that it relieved headaches. For example, in *CX 310* approximately 4% of consumers recalled Excedrin's advertising claiming it "relieves pain" (CX 310 Z091). In *CX 326*, 6% recalled that Bufferin relieves "headaches," and 4% recalled it relieves "pain" (CX 3260). Approximately 8% recalled Excedrin relieves "headaches" and 5% recalled it relieves "pain" (CX-326Z001). In *CX 345*, 4.3% recalled "relieves headaches," and 10.9% recalled "relieves pain" for Bufferin (CX 345Z057). For Excedrin, 8.2% recalled "relieves pain" and 7.1% recalled "relieves headaches" (CX 345Z066). The magnitude of recall of superior efficacy and tension relief claims shown in Tables III and IV should be judged against the context of low levels of recall for general claims (Ross, Tr. 7315-16; 7329; 7330; 7444-46; 7450-51).

726. The advertising penetration data in evidence demonstrates that substantial numbers of consumers remembered Bufferin's superior speed and superior gentleness claims and

Excedrin's superior effectiveness and tension relief claims. More than one-third of the consumers interviewed could recall Bufferin advertising; likewise more than one-third interviewed recalled Excedrin advertising off the tops of their heads on an unaided basis. Among those claims recalled, superiority in terms of speed and gentleness to the stomach were the dominant themes played back for Bufferin and strength and effectiveness were the dominant themes played back for Excedrin (F. 723-25, *supra*; Ross, Tr. 7194-95; 7205).

Table III

Unaided Advertising Penetration Based Upon Respondents Who Recalled Any Advertising For Bufferin

CX-310 (1969)[1]		CX-326 (1971)[2]		CX-345 (1973)[3]	
Works Twice As Fast/Faster Acting	42%	**Speed**	**38%**	Faster Acting	23.4%
		Faster/Goes To Headache Faster/twice as fast/in half the time	24%		
		Dissolves Faster	8%		
		Fast	8.1%		
Doesn't Effect/ Upset Stomach	21%	**Stomach**	**22%**	Doesn't Upset Your Stomach	14.7%
		Less Stomach Upset	3%	Relieves Stomach Discomfort	2.2%
		No Stomach Upset	16.2%		
It's Buffered/ Contains Buffering Agents	9.3%			More Buffers, Buffered	4.9%
				Tension/relieves tension	1.1%

[1]CX 310Z-094; Ross, Tr. 7171-7172.

[2]CX 326O, P, Q; Ross, Tr. 7187-7189.

[3]CX 345Z-057, 058, 107, Ross, Tr. 7193-7194.

Table IV

Unaided Advertising Penetration Based Upon Respondents Who Recalled Any Advertising For Excedrin

CX-310 (1969)[1]		CX-326 (1971)[2]		CX-345 (1973)[3]	
		Competitive Superiority	**45.5%**		
Extra-Strength Pain Reliver	4.5%	Stronger	20.5%	Stronger/Extra Strength	12.6%
Extra-Strength/ Stronger	12.1%	More Relief	2.3%	More Effective Than Aspirin	4.4%
Relieves Headaches/All Kinds of Headaches	13%	Generally Better More Ingredients	9.1% 4.5%		
Longer Lasting	3%				
Relieves Tension/ Nerves/Tension Headaches	10.6%	Tension	2.3%	Relieves Tension	2.7%

[1] CX-310Z091; Ross, Tr. 7196-7197.

[2] CX-326Z, Z-001; Ross, Tr. 7202-7203.

[3] CX-345Z066,-067,-107, Ross, Tr. 7204-7205.

C. Consumers In Substantial Numbers Believe Bufferin and Excedrin Are More Effective Than Aspirin

727. Six reliable market surveys in evidence, conducted during the period 1967 through 1975, demonstrate that a substantial number of consumers have believed and continue to believe that Bufferin is faster and gentler than aspirin and Excedrin is a more effective pain reliever than aspirin.

728. In a category of products such as OTC analgesic drugs, when consumers believe that the attributes of a particular OTC analgesic make it more efficacious than another product, they also believe that the superiority of that product on those attributes has been supported by adequate scientific evidence (Ross, Tr. 7055). As Dr. Ross testified:

[It's] reasonable in my judgment for consumers in not insignificant numbers to believe you must have such evidence lurking around or being the basis for such claims or you won't be allowed to make them (Ross, Tr. 7053).

729. The fact that typical marketing research, such as the surveys in evidence in this record, does not ordinarily report the nature or adequacy of scientific support underlying consumer beliefs about the attributes of products does not undermine Dr. Ross' view that consumer beliefs include a component relating to the adequacy of scientific support. Consumer research is not structured to pick up the existence of such a belief, nor do consumers ordinarily express the fact that there is underlying scientific support which led them to hold a belief (Ross, Tr. 7054-55).

730. Thus, despite the absence of explicit survey evidence, it is reasonable to infer, from survey evidence showing that consumers do believe in the claims that Bufferin is faster or gentler, or that Excedrin is stronger or more effective, that they also believe that there is adequate scientific support for these comparative claims.

1. *Evidence From Commercial Market Research Conducted in 1967 and 1970*

731. An image study tests the competitive position of one product versus another by measuring images or beliefs, and

the extent of those beliefs, about a product (Ross, Tr. 7224-25). These images or beliefs can be analyzed first by identifying those attributes which are pertinent to consumers' perceptions of the product and its benefits, and second by measuring the extent to which consumers believe those attributes are relevant to their purchasing decisions (Ross, Tr. 7224-25). One cannot learn the nature of consumer beliefs about a product from their purchases alone. In order to learn the nature of a consumer's beliefs about a product and its attributes one has to ask the consumer for a descriptive statement about those beliefs (Ross, Tr. 7226). The five studies (CX 1058, CX 346, CX 310, CX 1059 and CX 347-348), which were conducted at different times between 1967 and 1970 by different research organizations, for different OTC analgesics manufacturers (before the FTC Analgesics Complaints were issued in 1972), using different methodologies and different samples, provide relevant information for coming to a conclusion about the comparative images of both Bufferin and Excedrin relative to aspirin (Ross, Tr. 7229). All five studies are typical of the kinds of studies conducted in market research, and are of greater scope and higher reliability than many studies on attitude and image research that are used as a basis for marketing decisions by business firms (Ross, Tr. 7229- 30).

732. Due to the fact that these five studies focus on major branded analgesics and not unbranded "aspirin" the only way to assess consumers' beliefs about comparative effectiveness of Bufferin, Excedrin and aspirin is to use a surrogate for "aspirin": Bayer (Ross, Tr. 7240-41). This method injects a bias which tends to diminish differences in consumer beliefs about the branded aspirin products (Ross, Tr. 7401-02). This bias results from the fact that Bayer is both a well known, heavily advertised, widely used analgesic (Ross, Tr. 7241).

733. The five studies conducted between 1967 and 1970 report the results based upon the entire sample surveyed and upon the users of each brand. Three of these studies (CX 346, CX 310 and CX 347-348) also permit analyses of respondents who do not use, or do not regularly use, Bufferin, Excedrin, or Bayer (Ross, Tr. 7231-32).

734. An analysis that separately compares users' beliefs and nonusers' beliefs is preferable to an analysis that simply compares the beliefs of all respondents who gave their opinions about the efficacy of the products, regardless of their usage patterns (Ross, Tr. 7237). Preference for a "user v. user" or "non-user v. non-user" analysis is based upon the fact that the relative rather than the absolute beliefs and images are the subjects of concern in this proceeding. An analysis based on the results of the total sample builds in a bias that obscures relative beliefs and images (Ross, Tr. 7233-38; CX 822A).

735. The bias built in a total sample analysis is a consequence of the well recognized phenomenon that users of a product are apt to rate it more favorably than do nonusers (Ross, Tr. 7233). This bias, called user bias or user "halo," disproportionately favors Bayer, the brand that was used more often than Bufferin or Excedrin by the total population at the time the studies were done. Since there were many more Bayer users in the total sample of consumers surveyed than there were users of the challenged brands, the percentage of the total sample that said favorable things about Bayer can be expected to be disproportionately higher (Ross, Tr. 7401-02). This disproportionate usage of Bayer resulted in more frequent favorable ratings of Bayer by the total sample, and it obscured the relative beliefs — the true differences in beliefs — about Bufferin or Excedrin and Bayer (Ross, Tr. 7233, 7401-02). Separate analysis of relative beliefs among users of these products, and among nonusers of these products, balances the effects of Bayer users' favorable ratings of their product (Ross, Tr. 7234-7238). This technique is frequently used to hold constant the effects of differential product usage within a sample on the relative images of two brands (Ross, Tr. 7237-38; 7243).

736. None of the commercial image studies explicitly questioned consumers about the general pain relieving "efficacy" of the analgesics studied. However the attribute of strength has been shown to have a strong, logical relationship to a pain reliever's "effectiveness" (Ross, Tr. 7056-59).

736a. Tables V and VI compare users' beliefs of the product

attributes "speed" and "gentleness," respectively, for Bufferin and Bayer. Table VII displays a similar user belief comparison for Excedrin and Bayer with respect to a number of strength- and efficacy- related attributes. All three tables were derived from the five commercial image studies in evidence that were conducted during the period 1967-1970. They show that, during that period, a significantly greater portion of Bufferin users believed Bufferin was fast/gentle than Bayer users believed Bayer was, and a signifiantly greater portion of Excedrin users believed Excedrin was stronger or more effective than Bayer users believed Bayer was.

737. Results from three of the five studies done between 1967 and 1970 (CX 346, CX 310, CX 347-348) were also analyzed from the point of view of respondents who were not current users or current "most often" users of a brand. These results are shown in Tables VIII, IX and X, *infra*. This "non-users" analysis was another effort to remove, to the extent possible, the favorable bias that affects the ratings of all brands by virtue of the fact that those who rate them are also users of them. Analysis of beliefs and images among "non-users" removes this bias by actually removing the favorably biased users' ratings from the analysis. This contrasts with the "user v. user" analysis discussed in F. 735-736a, *supra*, which holds the bias constant by limiting the analysis to users' ratings (Ross, Tr. 7238).

738. Another advantage of the analysis of comparative beliefs and images among nonusers is that it more directly addresses the role of advertising as a source of the beliefs and images analyzed. By definition the opportunity for usage, or prior experience, to contribute to the comparative images of "non-users" is diminished or eliminated (Ross, Tr. 7238). As with the results of the user analyses presented in Tables V, VI and VII, "non-users" of Bufferin and Bayer believe Bufferin superior in speed and gentleness to Bayer; Excedrin and Bayer nonusers believe Excedrin superior in strength and pain relieving efficacy to Bayer.

Table V
Beliefs About Bufferin And Bayer
Percentages Based Upon Users Of Each Product
Speed

1967 CX-1058[1]	1967 CX-346[2]	1969 CX-310[3]	1970 CX-1059[4]	1970 CX-347/348[5]
Buf./Bayer	**Buf./Bayer**	**Buf./Bayer**	**Buf./Bayer**	**Buf./Bayer**
For Fast Relief	Relieves Pain Most Quickly	Speedy	For Fast Relief	Gives Fast Acting Relief
59.2/55.2% (N.S.)	73/65% (N.S.)	77/67%***	67.7/55.6%*	68.4/65.2% (N.S.)

[1] CX-1058Z486; CX-807Z101; Ross, Tr. 7269-7270; CX-822L. Dr. Ross' analysis was based upon the responses of males and females. The percentages displayed above simply combine those responses into a total percentage for Bufferin and Bayer users.

[2] CX-346Z150,-151; Ross, Tr. 7245, CX-822B.

[3] CX-310Z148,-071,-072; Ross, Tr. 7267, CX-822K.

[4] CX-1059Z233,-257; CX-807Z101; Ross, Tr. 7269-7270, CX-822L. See Footnote 1 *supra* regarding the meanings of these percentages.

[5] CX-348Z225,-229 (CX-347Z126); Ross, Tr. 7260, CX-822H.

N.S. = Sig.$<$.05
* = Sig.$>$.05
** = Sig.$>$.01
*** = Sig.$>$.001

Table VI
Beliefs About Bufferin And Bayer
Percentages Based Upon Users Of Each Product
Gentleness

1967 CX-1058[1]	1967 CX-346[2]	1969 CX-310	1970 CX-1059[3]	1973 CX-347/348[4]
Buf./Bayer	**Buf./Bayer**	**Buf./Bayer**	**Buf./Bayer**	**Buf./Bayer**
Doesn't Upset The Stomach	Never Upsets Stomach	N.A.	Doesn't Upset The Stomach	Never Upsets Stomach
76/66.5%*	67/68% (N.S.)		81.5/68.4%**	59.6/32%***
Irritates The Stomach			Irritates The Stomach	
4.6/9.3% (N.S.)			1.6/13.5%***	

[1] CX-1058Z481,-491; CX-807Z101; Ross, Tr. 7269-7270, CX-822L. Dr. Ross' analysis was based upon the responses of males and females. The percentages displayed above simply combine those responses into a total percentage for Bufferin and Bayer users.

[2] CX-346Z150,-151; Ross, Tr. 7245, CX-822B.

[3] CX-1059Z226,-250, CX-807Z101; Ross, Tr. 7269-7270, CX-822L. See Footnote 1 *supra* regarding the meanings of these percentages.

[4] CX-348Z225,-229 (CX-347Z126); Ross, Tr. 7260, CX-822H.

N.S. = Sig.$<$.05
* = Sig.$>$.05
** = Sig.$>$.01
*** = Sig.$>$.001

Table VII
Beliefs About Excedrin And Bayer
Percentages Based Upon Users Of Each Product

1967 CX-1058[1]	1967 CX-346[2]	1969 CX-310[3]	1970 CX-1059[4]	1970 CX-347/348[5]
Exc./Bayer	Exc./Bayer	Exc./Bayer	Exc./Bayer	Exc./Bayer
For Fast Relief 70.1/55.2%**	Relieves Pain Most Quickly 88/65%***	Speedy 85/67% (N.S.)	For Fast Relief 78.9/55.6%***	Gives Fast Acting Relief 78.7/65.2% (N.S.)
Gives Long Lasting Relief 74.9/53.1%***	Relieves Pain For A Long Period 71/44%***	Long Lasting 62/33% (N.S.)	Gives Long Lasting Relief 76.7/55.6%***	Gives Longer Lasting Relief 60.0/35.2%***
Good For Severe Headaches 75.9/47.9%***	Good For Severe Headaches 77/52%***	Mainly For Severe Headaches 35/7%(N.S.)	Good for Severe Headaches 72.2/48.1%***	Good For Severe Headaches 69.0/39.9%***
	Very Strong Product 75/37%***	Too Strong 3/1% (N.S.)	Extra Strength 82.7/19.5%***	Is Extra Strength 64.5/12.3%***
Strong 69.5/19.1%***			Strong 73.7/27.1%***	
Gives Complete Relief 69.5/51.0%***		Complete Relief 49/31%(N.S.)	Gives Complete Relief 69.9/57.1%*	

[1] CX-1058 Z478,-480,-485,-486,-490,-491; Ross, Tr. 7430-7431, CX-823N.
[2] CX-346 Z152,-153; CX-823A.
[3] CX-310 Z148,-071,-072; Ross, Tr. 7427-7430, CX-823M.
[4] CX-1059 Z226,-229,-233,-238,-241,-245 (CX-344 Z101); Ross, Tr. 7430-7432, CX-823N.
[5] CX-347 Z126, CX-348, Z225,-226,-233,-244; Ross, Tr. 7410-7411, CX-823H.

N.S. = Sig. $<$ .05
* = Sig. $>$ .05
** = Sig. $>$ .01
*** = Sig. $>$ .001

Table VIII
Beliefs About Bufferin And Bayer
Percentages Based Upon Non-Users Of Each Product
Speed

1967 CX-346[1]	1969 CX-310[2]	1970 CX-347/348[3]
Buf./Bayer	Buf./Bayer	Buf./Bayer
Relieves Pain Most Quickly	Speedy	Gives Fast Acting Relief
29/26% (N.S.)	61/48%***	42.6/41.1% (N.S.)

[1] CX-346Z059,-060,-150,-151; Ross, Tr. 7249, CX-822C.

[2] CX-310Z148,-071,-072; Ross, Tr. 7267, CX-822K. Percentages are based on beliefs about Bufferin by Bayer users, and vice versa.

[3] CX-348Z225,-229 (CX-347Z126); Ross, Tr. 7260, CX-822H.

N.S. = Sig.$<$.05
* = Sig.$>$.05
** = Sig.$>$.01
*** = Sig.$>$.001

Table IX
Beliefs About Bufferin And Bayer
Percentages Based Upon Non-Users Of Each Product
Gentleness

1967 CX-346[1]	1969 CX-310	1970 CX-347/348[2]
Buf./Bayer	**Buf./Bayer**	**Buf./Bayer**
Never Upsets Stomach	N.A.	Never Upsets Stomach
39/43% (N.S.)		35.3/16.5%***

[1] CX-346Z059,-060,-150,-151; Ross, Tr. 7249, CX-822C.

[2] CX-348Z225,-229 (CX-347Z126); Ross, Tr. 7260, CX-822H.

N.S. = Sig.<.05
* = Sig.>.05
** = Sig.>.01
*** = Sig.>.001

Table X
Beliefs About Excedrin And Bayer
Percentages Based Upon Non-Users Of Each Product

1967 CX-346 [1]	1969 CX-310 [2]	1970 CX-347/348 [3]
Exc./Bayer	**Exc./Bayer**	**Exc./Bayer**
Relieves Pain Most Quickly 25/26% (N.S.)	Speedy 61/36%*	Gives Fast Acting Relief 46.0/41.1%*
Relieves Pain for a Long Period 21/21% (N.S.)	Long Lasting 43/23%(N.S.)	Gives Longer Lasting Relief 27.2/17.9%***
Good for Severe Headaches 38/29%**	Mainly for Severe Headaches 39/4%(N.S.)	Good for Severe Headaches 38.4/25.6%***
Very Strong Product 33/15%***	Too Strong 25/2%(N.S.)	Is Extra Strength 40.3/11.6%***

[1] CX-346Z060,-061,-062,-066; Ross, Tr. 7404-7405, CX-823B.

[2] CX-310Z148,-071,-072; Ross, Tr. 7424, CX-823M. Percentages are based on beliefs about Excedrin by Bayer users, and vice versa.

[3] CX-347Z126, CX-348Z225,-226,-233,-244; Ross, Tr. 7140-7411, CX-823H.

N.S. = Sig.$<$.05
* = Sig.$>$.05
** = Sig.$>$.01
*** = Sig.$>$.001

739. CX-346, the 1967 *Assets & Liabilities Study*, is the only one of the five 1967-1970 studies which permits a comparison of both Bufferin's image and Excedrin's image with that of an "aspirin" product other than Bayer. While Bayer ratings were also included in the study and analyzed (Tables V through X) respondents were asked to rate Norwich and "store's own brand" as well on the same dimensions as Bufferin and Excedrin. These comparisons further confirm the superior speed and gentleness image of Bufferin and the superior strength and effectivensss image of Excedrin (F. 740, *infra*; Tables XI, XII; Ross, Tr. 7252-53, 7404-05).

740. An analysis of the nonexclusive users of Bufferin, Excedrin, Norwich and store's own brand aspirin in the 1967 *Assets and Liabilities Study* (CX 346) demonstrates that Bufferin's image is superior to Norwich's and store brand's images on the relevant attributes speed and gentleness and Excedrin's image is superior to Norwich and store's own brand on speed, strength and severe headache (Ross, Tr. 7250-53, 7404-05, Tables XI, XII).

741. Additional data from the *1969 Excedrin Study* (CX 310) provide "reasons for using" Bufferin and consequently support the results relating to beliefs about pertinent attributes of the product (Tables V, VI, IX). First, the most important performance element Bufferin users gave as their reason for initial trial of the product was "safety" (19% including references to stomach upset) (CX 310Z060). Further, of all of the reasons stated for switching to Bufferin, the three that stood out most were "no upset stomach" (23%). "saw/heard advertising" (17%), and "faster acting" (13%) (Ross, Tr. 7264-66; CX 310Z067-068; CX 822J). These respondents believed Bufferin to be a speedier product that was gentler to the stomach than the brand they previously used (Ross, Tr. 7264-65) and a substantial portion attributed their reason for switching to their brand to the images they formed from the "advertising" they saw for Bufferin (Ross, Tr. 7265-66).

742. The *1970 Vanquish Study* (CX 347-348) reports additional data to support the fact that people used their particular brands to obtain benefits that were consistent with the benefits

they sought from a headache remedy in general (Ross, Tr. 7258-59). That is, Bufferin users, to a significant degree more than Bayer users, believed that "contains buffers" (60.3%/11.9%) and "doesn't upset your stomach" (84.6%/75.9%) were reasons for using their brand; and Bufferin users, to a significant degree more than Bayer users (32%/2.4%) stated "doesn't upset stomach/buffers" was a reason for using their regular brand specifically "most often for headaches" (Ross, Tr. 7258-59). These data demonstrate that Bufferin users chose their brand because they believed it was gentler to the stomach than aspirin, *i.e.*, it would prevent or diminish stomach upset (Ross, Tr. 7258-7259). This study also shows that Bufferin users more often than Bayer users believe that "headache remedies and pain relievers work too slowly," indicating that users of Bufferin are convinced that some brands work faster than others, and that this is their reason for choosing Bufferin over other brands.

TABLE XI
Beliefs About Bufferin and Aspirin
Percentages Based Upon Non-Exclusive Users of Each Brand

1967 CX-346[1]	Buf./Norwich/Store
Relieves Pain Most Quickly	15/5/1%
Never Upsets Stomach	23/12/11%

[1] CX-346Z059, -060; Ross, Tr. 7252-7253; CX-822E.

Table XII
Beliefs About Excedrin and Aspirin
Percentages Based Upon Non-Exclusive Users of Each Brand

1967 CX-346[1]

Exc./Norwich/Store

Relieves Pain Most Quickly
21/5/1%

Relieves Pain For A Long Period
16/2/-1%

Very Strong Product
27/2/-3%

Good For All Kinds of Pain
16/11/7%

Good For Severe Headaches
31/6/3%

[1] GX-346Z060, -061, -062, -064, -066; Ross, Tr. 7404-7405; CX-823C, D.

743. Results of the 1969 *Excedrin Study* (CX 310) demonstrate that Excedrin users use their brand for the precise attributes which it advertises: comparative strength and effectiveness. Of all the reasons cited for switching to Excedrin, "faster acting" (37%) and "stronger, more powerful" (19%) were the most frequent reasons given by Excedrin users (Ross, Tr. 7417-18; CX 823K). Moreover, a substantial portion of Excedrin users (16%) listed "saw/heard advertising" as their reason for switching to Excedrin, and 44% cited advertising as their reason for coming to Excedrin in the first place. Excedrin users claim to suffer from "severe headaches" far more than Bayer users do (50%/24%). This represents the largest difference for ailments treated by users of the two brands (Ross, Tr. 7420-23; CX 823L). Excedrin users, more than Bayer users (93%/59%), chose their own brand for treatment of "severe headaches"; and Bayer users were far more inclined to use Excedrin for "severe headaches," than were Excedrin users inclined to take Bayer (13%/1%) (Ross, Tr. 7424, CX 823L). These data show that both Excedrin and Bayer users believe

Excedrin is a stronger pain reliever than aspirin, and that Excedrin users suffer from, and use their brand to relieve, specifically those ailments for which it advertises relief (Ross, Tr. 7420-24). Further, Excedrin users claim to suffer from ailments which reflect greater pain than do Bayer users, *e.g.*, twice as many Excedrin users than Bayer users felt that their "headaches are more severe than other people's headaches"; and six times as many believed, "Headache remedies and pain relievers don't work for me unless they are extra strong." Accordingly, Excedrin users think their brand contains what they want in an analgesic — extra strength (Ross, Tr. 7420-23).

744. The *1970 Vanquish Study* (CX 347-348) demonstrates further that Excedrin users use their brand for the attributes it advertises. The most frequent reasons why Excedrin users used their brand most often for headaches were "gives fast/quick relief" (28.8%), "works faster than others" (18.2%) (Ross, Tr. 7407-08; CX 823F). Of the reasons for using "headache remedies," those which stood out the most for Excedrin users were "provides quick relief" (90.3%), "be extra strong" (57.4%), "stronger than plain aspirin" (64.5%), and "provides long lasting relief" (85.2%) (Ross, Tr. 7408-10; CX 823F). Other opinions reveal that Excedrin users, more than Bayer users, believe some brands work faster than others, and other brands work too slowly (Ross, Tr. 7412-13; CX 8231). These data indicate again that Excedrin users want and believe their brand has superior speed, strength and effectiveness, over other brands (Ross, Tr. 7414-17).

2. *Evidence Of Current Consumer Beliefs In Bufferin's And Excedrin's Superiority Is Supplied By The Leavitt Study CX 349*

745. The Leavitt Study was an adequately designed, carefully administered consumer study performed for the Federal Trade Commission's staff by Dr. Clark Leavitt and the Gallup Organizaton. The study was a telephone survey which employed well-controlled, reasonably randomized procedures to contact 780 consumers, who were asked to rate the pain reliev-

ing efficacy, speed, strength and gentleness of aspirin, Anacin, Bufferin and Excedrin.

746. Approximately 98% of the 780 respondents interviewed by Gallup Organization had heard of all of the four products surveyed. Dr. Leavitt did not analyze data from the 17 respondents, or 2%, who had not heard of all of the survey products (Leavitt, Tr. 6199). This was a reasonable approach (Leavitt, Tr. 6191-95). The exclusion of these seventeen (17) respondents did not impact upon the reliability of Dr. Leavitt's analysis because, in fact, analyses of results based upon all 780 interviews produced results virtually identical to those obtained when the 17 were excluded (F. 756, *infra*).

747. Whenever a respondent was unwilling or unable to rate a production the four-point scale presented to him in Questions 2 through 5, the interviewer was instructed to code "Don't Know" on the questionnaire (Leavitt, Tr. 6185; CX 349W). The pretesting of the questionnaire had disclosed that some respondents might be unwilling to rate a product because they did not personally use it (Crespi, Tr. 2270) and the questionnaire was modified to address this possibility by changing the preamble to Questions 2 through 5 to begin "Whether or not you have ever used them ...." During the actual interviews respondents' reasons for not rating a product were not sought out by the interviewers who had been instructed not to deviate from or to explain the wording on the questionnaire — only to repeat it (F. 165, *supra*).

748. Comparing a consumer's images about different products is an acceptable alternative to eliciting a statement of his own comparative images of these products. The former approach has an important advantage in that it permits an analysis of the degree or intensity of the comparative perceptions underlying a direct comparative statement. The Leavitt Study adopted the former approach and differs from the five commercial marketing studies in evidence in this respect.

749. Comparative beliefs in the Leavitt Study are assessed by confining analysis to those respondents who expressed an opinion about both Bufferin or Excedrin and aspirin (Ross, Tr.

7279-80). This approach is based upon the view that a "Don't know" response about Bufferin or Excedrin, on the one hand, or about aspirin, on the other, reflects the lack of a basis for any comparative image concerning the three products (Ross, Tr. 7279-80). Therefore, exclusion of "Don't know" responses from an analysis of comparative images is appropriate for two reasons: (1) a "Don't know" response, by definition, is a lack of opinion; and (2) it is virtually impossible to position a "Don't know" response on the four point scale along with "extremely," "very fairly" and "not" (Ross, Tr. 7279-80). This was a reasonable approach.

750. While inclusion of "don't know" responses as part of an analysis of comparative images is not as meaningful and may lead to erroneous conclusions, Dr. Ross analyzed the data from the Leavitt Study based on both the total sample, including "Don't knows," and the subsample of respondents who rated both products (*i.e.*, excluding "Don't knows") (Ross, Tr. 7279). These dual analyses were performed to see if conclusions about comparative images differed depending upon the approach adopted (Ross, Tr. 7280).

751. When expressed as percentages based upon all 763 respondents analyzed by Dr. Leavitt in CX 349, the raw results are depicted in Tables XIII and XIV, *infra*. There are four "independent" percentages in each row of these tables, *i.e.*, the percentages in each row represent completely independent groups of respondents, and each response appears once, and only once, in each row (Crespi, Tr. 2352; Leavitt, Tr. 6203-04). These percentages are reasonably projectable to the population of adults who live in homes with telephones and who are aware of these products (Leavitt, Tr. 6193; 6246-47). At the 95% level of confidence, given a sample of approximately 750 people, the percentages could vary by approximately plus or minus 4% (Crespi, Tr. 2346-47). These results, generally speaking, show that approximately one out of every four Americans in telephone households who are aware of these products believes Bufferin is faster and gentler than aspirin and that Excedrin is more effective than aspirin.

752. Tables XV and XVI show the same comparative beliefs, but the percentages are based upon the subsample who rated both products as indicated. Regardless of the sample base used, Tables XIII-XVI clearly demonstrate that a significant number of consumers believed Bufferin was faster and gentler than aspirin, and Excedrin is faster, stronger and more effective than aspirin (Ross, Tr. 7435-36; CX 822M; CX 823P).

Table XIII
Beliefs About Bufferin And Aspirin
Percentages Based Upon The Total Sample[1]

	Rated Both Products			Did Not Rate Both Products[2]	
	Rated Bufferin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Bufferin		Total
Speed	22.4%(171)	28.7%(219)	5.4%(41)	43.5%(332)	763 = 100%
Gentleness	24.9%(190)	28.1%(214)	7.2%(55)	39.8%(304)	763 = 100%

[1] CX-349Z018,-019; Ross, Tr. 7273-7275; CX-822M.

[2] Respondents were coded "Don't Know" for either Bufferin, aspirin or both.

Table XIV
Beliefs About Excedrin And Aspirin
Percentages Based Upon The Total Sample[1]

	Rated Both Products			Did Not Rate Both Products[2]	Total
	Rated Excedrin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Excedrin		
Effectiveness	22.1%(169)	25.0%(191)	3.7%(28)	49.2%(375)	763 = 100%
Speed	25.2%(192)	20.5%(156)	4.2%(32)	50.2%(383)	763 = 100%
Strength	23.6%(180)	22.5%(172)	2.8%(21)	51.1%(390)	763 = 100%

[1] CX-349Z015,-016,-017; Ross, Tr. 7435-7436; CX-82[illegible]P.

[2] Respondents were coded "Don't Know" for either Excedrin, aspirin or both.

Table XV
Beliefs About Bufferin and Aspirin
Percentages Based Upon The Total Sample Who Rated both Products[1]

	Rated Bufferin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Bufferin	Total
Speed	39.7%(171)	50.8%(219)	9.5%(41)	431 = 100%
Gentleness	41.4%(190)	46.6%(214)	12.0%(55)	459 = 100%

[1] Table XIII.

Table XVI
Beliefs About Excedrin And Aspirin
Percentages Based Upon The Total Sample Who Rated Both Products[1]

	Rated Excedrin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Excedrin	Total
Effectiveness	43.6% (169)	49.2% (191)	7.2 (28)	388 = 100%
Speed	50.5% (192)	41.1% (156)	8.4 (32)	380 = 100%
Strength	48.3% (180)	46.1% (172)	5.6 (21)	373 = 100%

[1] Table XIV.

753. Tables XVII and XVIII reflect the comparative images of Bufferin and aspirin, and Excedrin and aspirin, respectively, among the nonusers of Bufferin and Excedrin who rated both brands. Since a comparison of nonusers removes user bias with respect to Bufferin and Excedrin the comparisons shown in Tables XVII and XVIII are more conservative than those shown in Tables XIII-XVI (Ross, Tr. 7274-75; 7435-36). In any event, Tables XVII and XVIII also demonstrate that a substantial number of consumers believed Bufferin is faster and gentler than aspirin and that Excedrin is superior to aspirin in terms of speed, strength and effectiveness (Ross, Tr. 7273-78; 7435-36; CX 822M, CX 823P). *Cf.* Tables XIX-XXII, *infra*.

754. Tables XIX and XX reflect the comparative images of all those respondents who used *neither* Bufferin *nor* aspirin or who used *neither* Excedrin *nor* aspirin. Tables XXI and XXII reflect the images among the same subsample, but percentages are based upon those who rated both products only (Ross, Tr. 7290-98; 7302; 7437; 7439-40). The analysis reflected in Tables XIX-XXII removes user bias completely because it removes aspirin usage as well as usage of Bufferin and Excedrin. Thus, their analysis reflects the prevalence and nature of comparative images among those persons who had images which by definition could not be affected by usage (F. 738, 753, *supra*; Ross, Tr. 7284-85). The results demonstrate that a significant number of this subsample of respondents believe that Bufferin is faster and gentler than aspirin, and that Excedrin is faster, stronger and more effective than aspirin regardless of whether the percentage base includes the "Don't knows" (Ross, Tr. 7296, 7300-02, 7437, 7439-7400).

755. Finally, Tables XXIII through XXVI reflect the comparative images of nonusers of all four products surveyed in the Leavitt Study. This analysis is even more conservative in terms of eliminating all possible sources of user bias. The results in Tables XXIII-XXVI also demonstrate for both Bufferin and Excedrin that their superior image over aspirin persists in this most conservative analysis (Ross, Tr. 7298-7300, 7303, 7438, 7440).

756. As indicated in Table XXVII, the fact that Dr. Leavitt discarded data from seventeen (17) respondents who were not aware of all four products surveyed has no impact upon the results of this study. A comparison of results based upon either the 763 respondents analyzed by Dr. Leavitt or all 780 respondents interviewed reveals virtually identical results.

Table XVII
Beliefs About Bufferin And Aspirin
Percentages Based Upon Non-Users Of Bufferin
Who Rated Both Products[1]

	Rated Bufferin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Bufferin	Total
Speed	28.5% (63)	59.7% (132)	11.8% (26)	221 = 100%
Gentleness	29.3% (71)	55.8% (135)	14.9% (36)	242 = 100%

[1] CX-349Z018,-019; Ross, Tr. 7273-7278; CX-822M.

Table XVIII
Beliefs About Excedrin And Aspirin
Percentages Based Upon Non-Users Of Excedrin
Who Rated Both Products[1]

	Rated Excedrin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Excedrin	Total
Effectiveness	28.1% (65)	61.5% (142)	10.4%(24)	231 = 100%
Speed	36.7% (80)	55.5% (121)	7.8%(17)	218 = 100%
Strength	39.1% (88)	49.3% (111)	11.6%(26)	225 = 100%

[1] CX-349Z015,-016,-017; Ross, Tr. 7435-7436; CX-823P.

Table XIX
Beliefs About Bufferin And Aspirin
Percentages Based Upon Non-Users Of Both Products[1]

	Rated Both Products			Did Not Rate Both Products	
	Rated Bufferin Higher Than Aspirin	Rated Bufferin Equal to Aspirin	Rated Aspirin Higher Than Bufferin		Total
Speed	16.9%(43)	26.4%(67)	1.6%(4)	55.1%(140)	254 = 100%
Gentleness	19.7%(50)	24%(61)	3.9%(10)	52.4%(133)	254 = 100%

[1] CX-349W,X (Qu. #2, 3, 9); Ross, Tr. 7290-7298; CX-8220,R.

Table XX
Beliefs About Excedrin And Aspirin
Percentages Based Upon Non-Users of Both Products[1]

	Rated Both Products			Did Not Rate Both Products	
	Rated Excedrin Higher Than Aspirin	Rated Excedrin Equal To Aspirin	Rated Aspirin Higher Than Excedrin		Total
Effectiveness	13.7% (41)	23% (69)	1.3% (4)	62% (186)	300 = 100%
Speed	16.3% (49)	19.7% (59)	1% (3)	62.3% (187)	300 = 100%
Strength	14.3% (43)	21% (63)	.7% (2)	64% (192)	300 = 100%

[1] CX-349W,X (Qu. #3,4,5,9); Ross, Tr. 7437-7439-40; CX-823R,U,X.

Table XXI
Beliefs About Bufferin And Aspirin
Percentages Based On Non-Users Of Both Products
Who Rated Both Bufferin And Aspirin[1]

	Rated Bufferin Higher	Rated Both The Same	Rated Aspirin Higher	Total
Speed	37.8%(43)	58.8%(67)	3.5%(4)	114 = 100%
Gentleness	41.3%(50)	50.4%(61)	8.3%(10)	121 = 100%

[1] Table XIX.

Table XXII
Beliefs About Excedrin And Aspirin
Percentages Based On Non-Users Of Both Products
Who Rated Both Excedrin And Aspirin[1]

	Rated Excedrin Higher	Rated Both The Same	Rated Aspirin Higher	Total
Effectiveness	36%(41)	60.5%(69)	3.5%(4)	114 = 100%
Speed	44.1%(49)	53.2%(59)	2.7%(3)	111 = 100%
Strength	39.8%(43)	58.3%(63)	1.9%(2)	108 = 100%

[1] Table XX.

Table XXIII
Beliefs About Bufferin And Aspirin
Percentages Based Upon Non-Users Of Aspirin, Bufferin, Excedrin, Or Anacin[1]

	Rated Both Products			Did Not Rate Both Products	
	Rated Bufferin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Bufferin		Total
Speed	18.7%(27)	22.9%(33)	1.4%(2)	56.9%(82)	144 = 100%
Gentleness	23.6%(34)	18.8%(27)	2.8%(4)	54.9%(79)	144 = 100%

[1] CX-349W,X (Qu. #2,9); Ross, Tr. 7298-7300, 7303; CX-822P,S.

Table XXIV
Beliefs About Excedrin And Aspirin
Percentages Based Upon Non-Users Of Aspirin, Bufferin Excedrin, Or Anacin[1]

	Rated Both Products			Did Not Rate Both Products	
	Rated Excedrin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Excedrin		Total
Effectiveness	14.6%(21)	18.1%(26)	.7%(1)	66.7%(96)	144 = 100%
Speed	11.1%(16)	22.2%(32)	1.4%(2)	65.3%(94)	144 = 100%
Strength	10.4%(15)	23.6%(34)	.7%(1)	65.3%(94)	144 = 100%

[1] CX-349W,X (Qu. #3, 4, 5, 9); Ross, Tr. 7438-7440; CX-823S,V,Y.

Table XXV
Beliefs About Bufferin And Aspirin
Percentages Based Upon Non-Users Of Aspirin, Bufferin, Excedrin, Or Anacin Who Rated Both Bufferin And Aspirin[1]

	Rated Bufferin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Bufferin	Total
Speed	43.6%(27)	53.2%(33)	3.2%(2)	62 = 100%
Gentleness	29.1%(34)	3.4%(4)	67.5%(79)	117 = 100%

[1] Table XXIII.

Table XXVI
Beliefs About Excedrin And Aspirin
Percentages Based Upon Non-Users Of Aspirin, Bufferin, Excedrin, Or Aspirin Who Rated Both Excedrin and Aspirin[1]

	Rated Excedrin Higher Than Aspirin	Rated Both The Same	Rated Aspirin Higher Than Bufferin	Total
Effectiveness	43.8%(21)	54.2%(26)	2.1%(1)	48 = 100%
Speed	12.0%(16)	64.0%(32)	4.0%(2)	50 = 100%
Strength	41.7%(15)	94.4%(34)	2.8%(1)	36 = 100%

[1] Table XXIV

Table XXVII
Comparison of Percentage Results Based Upon 763* and (780)** Respondents

Bufferin

	Bufferin Superior To Aspirin	Bufferin Equal To Aspirin	Aspirin Superior To Bufferin
Speed	22.4% (22.4%)	28.7% (29.1%)	5.4% (5.4%)
Gentleness	24.9% (24.9%)	28.1% (28.3%)	7.2% (7.2%)

Excedrin

	Excedrin Superior To Aspirin	Excedrin Equal To Aspirin	Aspirin Superior To Excedrin
Effectiveness	22.1% (22.1%)	25.0% (24.9%)	3.7% (3.9%)
Speed	25.2% (23.9%)	20.5% (20.4%)	4.2% (4.1%)
Strength	23.6% (23.6%)	22.5% (22.4%)	2.8% (2.7%)

* Tables XIII, XIV.
** Ross, Tr. 7273-7275, 7439-7441; CX-822Q,T; CX-823T,W,Z.

757. The Leavitt Study together with the five commercial image studies discussed in this section, provides convincing confirmatory evidence that a significant segment of the consuming public over the years has held the beliefs that Bufferin is faster and gentler than aspirin and Excedrin is faster and more effective than aspirin.

D. Respondent's Advertising Played A Substantial Role In Creating And Reinforcing Consumers' Beliefs In Their Superiority Over Aspirin

758. Several factors play a role in the creation and reinforcement of beliefs (often used interchangeably with "images") about products. Obviously, the most important factors are product usage and advertising (Ross, Tr. 7483-84, 7486). "word of mouth," is also recognized as a source of product beliefs. However, "word of mouth" is a derivative factor: it derives from product usage and advertising (Ross, Tr. 7484).

759. The fundamental role of advertising is to call consumer's attention to the attributes of a product and to create favorable expectations about the performance of that product (Ross, Tr. 7486-85, 7496). For consumers who have already tried the product, advertising serves to reinforce those expectations by reminding consumers about the benefits of the product (Ross, Tr. 7487). Hence, advertising plays an important role in both the initial trial of a product and continued use of the product (Ross, Tr. 7487).

760. It is difficult to distinguish between the role of advertising, on the one hand, and product usage, on the other, in creating beliefs about products (Ross, Tr. 7488). The extent to which product usage will act as a distinct source of a belief about a product depends upon the difference between consumers' perception of product performance and their ability to "evaluate" product performance (Ross, Tr. 7488-89). The perception of product performance simply refers to a consumer's description of his or her own perception of the use experience. In contrast, the ability to "evaluate" refers to the ability to accurately measure or assess the true performance and differences between products (Ross, Tr. 7489-90).

761. Advertising is less important as a source of beliefs, and usage more important, in those cases where consumers' usage experience permits them to "evaluate" a product's performance. Usage in such situations provides the opportunity to confirm or disconfirm the expectations about product performance induced by advertising (Ross, Tr. 7493). A pocket calculator is such an example.

762. On the other hand, when consumer use does not permit "evaluation" of true product performance, consumer beliefs are, to a significant degree, the result of expectations induced by advertising. In such cases, usage experience does not provide the opportunity to confirm or disconfirm the expectations about product performance that advertising induces (Ross, Tr. 7494). A drug is a good example. The inability of consumers to evaluate the true pharmacological performance of a drug is supported by classical psychological research which shows that user "perceptions" of the performance of drugs are significantly influenced not by actual product performance but by extraneous information such as advertising (Brock, Tr. 8557-58).

763. In the case of mild OTC analgesic products, such as Bufferin and Excedrin, product usage plays a minor role in creating product beliefs because consumer's ability to "evaluate" the pharmacological performance of the drug is affected by such factors as the placebo effect, the subjective nature of pain, and by the fact that each experience with pain is different. With respect to *comparative* product images of different OTC analgesics, usage is even less a factor as a source. In addition to the factors already named, consumers know the identities of the products they take for pain relief. Hence, their differential advertising-induced expectations for each product's performance operate to influence their "perceptions of these product's comparative performance. Consequently, consumers cannot "evaluate" the comparative performance of mild OTC analgesics on an unblinded basis (*i.e.*, when consumers know the products they are taking) (F. 399, *supra*).

764. Because consumers cannot "evaluate" the performance of OTC analgesics, their use experiences with the prod-

uct cannot serve to disconfirm advertising-induced expectations about product performance (Brock, Tr. 8598-8602). This makes advertising more important a factor than usage as a source of product images regarding OTC analgesic products. Consumer research studies in evidence and the testimony of experts support this conclusion.

765. Furthermore, the market research in evidence shows that both users and nonusers hold essentially the same beliefs about the performance attributes of Bufferin and Excedrin (F. 736a-40, 752-55, *supra*). This absence of a difference in belief structure between users and nonusers is further support for the conclusion that the advertising for Bufferin and Excedrin has played a significant role in creating and reinforcing beliefs about those products.

766. Bufferin's advertised attributes of superior speed and gentleness are important to consumers who choose Bufferin (CX 347Z039; Brock, Tr. 8692). The themes of superior speed and gentleness compared to aspirin have been important aspects of Bufferin's advertising since at least 1960 (CX 816; CX 800). Likewise, Excedrin's advertised attribute of superior effectiveness is important to consumers who choose Excedrin (CX 347Z039; Brock, Tr. 8695) and this theme has been an important aspect of Excedrin advertising since it was introduced around 1960 (CX 818; CX 801).

767. From 1960 to 1973, Bristol-Myers spent over $171 million advertising Bufferin and over $98 million advertising Excedrin (F. 5, *supra*). Advertisements disseminated during this period portrayed Bufferin as a product that was faster and gentler than aspirin and Excedrin as a more effective pain reliever than aspirin (CX 816; CX 818; CX 800; CX 801). During this period Bufferin's advertising-to-sales ratio was about 30% and Excedrin's about 32% (CX 660; CX 661). There is evidence that advertisements representing Bufferin as faster than aspirin were disseminated between 1950 and 1976 at least 6,122 times on national and/or spot television programs and at least 28 times in magazines with national circulations (CX 816; CX 800). There is evidence that advertisements representing Bufferin as gentler than aspirin were disseminated be-

tween 1961 and 1976 at least 5,569 times on national and/or spot television programs and at least 11 times in magazines with national circulations (CX 816; CX 800). From 1960 to 1976 advertisements representing Excedin as a more effective pain reliever than aspirin were disseminated at least 1,395 times on national and/or spot television programs and at least 116 times in magazines with national circulations (CX 818; CX 801H-801Z006).

768. The basic literature in both marketing and psychology shows that various well-known principles of persuasion can, if successfully used in communications, play a significant role in creating lasting beliefs, including beliefs about products (Brock, Tr. 8592-93). Dr. Brock, an expert in the applications of techniques of persuasion, analyzed a reasonably representative sample of Bufferin and Excedrin ads in evidence to ascertain the extent to which principles of persuasion were employed. He found a consistent and effective use of these techniques in them (Brock, Tr. 8593-96). Among the most prevalent techniques or principles known to be effective and used in the advertising of Bufferin and Excedrin are: (1) Linking a product with important human values. By linking the product with something important to the consumer (*e.g.*, relief from pain, maintenance of livelihood), the consumer is less likely to accept contrary information about the product, (2) The use of source credibility such as using medical experts or studies to support medical claims to enhance the believeability of the message, (3) Repetition (Brock, Tr. 8593- 95).

769. In fact, in the sample of Bufferin and Excedrin ads which were analyzed in detail in his testimony, Dr. Brock found frequent use of at least ten distinct principles of persuasion. Among them were (1) the linking of the product with an important human value (CX 34; CX 39A; CX 79A; CX 104; CX 717G; CX 125A CX 148; CX 729); (2) the use of highly credible sources such as doctors and medical reports (CX 3A; CX 78A; CX 79A; CX 717G; CX 153A; CX 164; CX 173; CX 176A; CX 204); (3) the repetition of claims or themes (CX 32A; CX 39A; CX 87A; CX 722; CX 153A); (4) the arousal of

an apparent conflict in the communication and then the offering of the product as the solution to this conflict; (CX 22A; CX 32A; CX 87A; CX 722; CX 162A); (5) the making of claims that cannot be refuted by the consumer through his experience (CX 22A; CX 32A; CX 39A; CX 74A; CX 87A); (6) the use of "open-minded manipulation," a technique designed to induce attitude formation or change by asking the viewer to consider the possibility of different points of view (CX 93); (7) the use of metaphors: that is, suggesting the product is like something else with which the viewer is familiar (CX 83); [6](8) endowing the commercials with trappings of scientific precision (CX 94; CX 132A; CX 729); (9) describing the message or product as being a scarce commodity making the message more valuable to consumers (CX 82; CX 153A; CX 164); and (10) presenting the product as successfully used by many other consumers ("social comparison principle") (CX 104; CX 148A) (Brock, Tr. 8597-8614, 8627-31). Dr. Brock found that repeated use of these principles of persuasion made product attributes both more salient and beliefs about them more stable in the minds of consumers (Brock, Tr. 8614).

770. There are several methods of ascertaining whether the use of persuasion techniques in advertising have been successful in creating a lasting impact on consumers. These methods include analysis of consumers' acceptance or other immediate reactions to advertising, analysis of the effect of advertising on consumers' intention to purchase or use the products, and analysis of any delayed impact or penetration of the advertising messages (Brock, Tr. 8614-15).

771. An important measure of the success of a communication is the extent to which an individual accepts it (Brock, Tr. 8615). Thus, it is important to look at consumers' immediate reaction to a communication, such as their own feelings of being convinced, informed, or persuaded by the message. Such measures indicate the extent to which the communication was effective in creating an impact in the form of beliefs (Brock,

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6 Dr. Brock referred to CX 94 as an illustration of the principle. CX 93 in evidence is identical to CX 94 (Brock, Tr. 8596-97).

Tr. 8615-16). The ASI copy tests in evidence measured in part consumers' reactions to Bufferin and Excedrin advertisements. Consumers were asked to select from a list of positive and negative adjectives that best described their feeling about the commercials they had just viewed. In doing so, consumers consistently found the tested commercials for Bufferin and Excedrin to be "informative," "convincing" and "effective." These results confirm the fact that the persuasive techniques used in the Bufferin and Excedrin ads were having an impact, and support the view that this advertising could reasonably be viewed as playing a significant role in forming beliefs about both Bufferin and Excedrin (Brock, Tr. 8619-21 8633-35).

772. Another important measure of the success of persuasion techniques in advertising is the extent to which it influences consumers' intentions to purchase the advertised product (Brock, Tr. 8614-15). The ASI copy tests in evidence also provide information that permits an analysis of the relation between advertising for Bufferin and Excedrin and purchase intention. In those ASI tests consumers were asked about their preferences for various analgesic products, both before and after they viewed various Bufferin and Excedrin commercials. The results showed a small increase in preference for Bufferin and Excedrin after viewing commercials (CX 828; CX 840; Brock, Tr. 8624, 8635). This increase is significant because of two factors operating against any change in preference at all: the desire to be consistent and the desire to resist the direction of persuasion (Brock, Tr. 8623).

773. An analysis of advertising penetration, or delayed impact also supports the role of advertising as an important factor in forming beliefs about Bufferin and Excedrin. The various advertising penetration studies in evidence demonstrate that a significant number of consumers remembered the superior speed and gentleness claims for Bufferin and the superior effectiveness claims for Excedrin off the top of their heads (F. 718-26, *supra*). Three of these penetration studies (CX 310, 325, 345) can be analyzed to ascertain the effects of advertis-

ing over time and whether advertising is influencing use of the product (Brock, Tr. 8638). Data from CX 310 shows that the advertising for both Bufferin and Excedrin was one of the most frequent reasons for initial trial of the product (CX 310Z60; Brock, Tr. 8639-40). Data from these three penetration studies also show that consumers in general had high awareness of the advertising for these products (CX 301Z090; CX 3250, Q, Z, Z001, CX 354V, W; Brock, Tr. 8640, 8647-48) and significant recall of the superior speed and gentleness claims for Bufferin and the superior effectiveness claims for Excedrin (CX 310Z90-95; Brock, Tr. 8641, 8645). These studies show a strong penetration of advertising themes for Bufferin and Excedrin, and a significant connection between the advertising and the beliefs about those products (Ross, Tr. 7510-11).

774. The Bufferin and Excedrin advertisements themselves, the ASI research, the advertising penetration studies and the expert testimony in this record taken together tend to confirm that the advertising for Bufferin played a substantial role in creating and reinforcing consumers' beliefs that Bufferin is gentler to the stomach and a faster pain reliever than aspirin and the belief that Excedrin is a more effective than aspirin (Brock, Tr. 8650; Ross, Tr. 7510-11).

E. The Evidence Regarding Tension Relief Image Of Bufferin, Excedrin and Excedrin P.M. Equivocal And Inconclusive

775. The tension relief claims for Bufferin, Excedrin and Excedrin P.M. began during the early 1960's and ceased by 1970, some 10 years ago. Tension relief claims for Excedrin ceased in 1969. The image studies in the record is equivocal and inconclusive on the issue of whether a substantial number of consumers hold "tension reliever" images regarding Bufferin or Excedrin. In these circumstances, it cannot be reasonably inferred from the fact of advertising dissemination a fact of tension relief image among consumers regarding Bufferin, Excedrin or Excedrin P.M.

776. Dr. Ross reviewed the image studies in evidence in this proceeding for the purpose of coming to a conclusion about the nature of people's images of Bufferin (Tr. 7227). Dr. Ross did *not* state that, in his opinion, such image of Excedrin as a tension reliever, which he felt to exist, was created or reinforced by Excedrin advertising. Dr. Ross did *not* state that, in his opinion, such image of Bufferin as a tension reliever, which he felt to exist, was created or reinforced by Bufferin advertising.

777. Dr. Brock reviewed the evidence relevant to the question of an image among consumers for tension relief for these products and declined to give an opinion because he found the evidence "unclear and sparse" (Tr. 8724-25). More people in the Leavitt Study (1.8%) stated that aspirin was good for the relief of tension than stated that either Bufferin (1.7%) or Excedrin (0.9%) was good for the relief of tension (Tr. 6219; CX 350Z008).

778. Dr. Ross admitted that the data indicate that not insubstantial numbers of consumers regard unadvertised plain or store brand aspirin as efficacious for the relief of tension (Tr. 8217-18, 8221). In fact, in a 1964 Gallup survey, 24% of the people surveyed stated that simple aspirin relieved nervous tension (CX 333K).

779. Dr. Ross claimed to find evidence for the existence of a consumer image of Bufferin as a tension reliever in the data collected in CX 345 (Tr. 7311-12). However, none of the data recorded in CX 345 have any relevance to Bufferin advertising because the only advertisements, which, in Dr. Ross' opinion, made tension relief claims (CX 816A-C) were run exclusively on the West Coast (CX 881O-W), and no sampling was done for CX 345 on the West Coast (Tr. 558; BMF 1220).

780. As part of the basis for his opinion that Bufferin has an image as a tension reliever Dr. Ross looked to the data contained in *C 310 at Z056 and Z072* (Tr. 7321-23). However, the interviewing for CX 310 was conducted during the period June 6, 1969 through July 20, 1969 (CX 310L) and the "Sensitive People" campaign did not begin running on the West Coast (CX 880W-881B; CX 881O-W) until mid-June

1969 (CX 800K-L). Thus, very few of the people interviewed for CX 310 could have seen that advertising and the few that might have seen it would have been exposed to it for, at most, one month. Dr. Ross also relied on CX 1058 and CX 1059 for his opinion regarding an image of Bufferin as a tension reliever and the source of that image. The data on which Dr. Ross relied for these two studies are summarized on CX 822V and W. Those data show that a tension relief image existed for Bufferin in 1967, prior to the Sensitive People campaign, and that image had actually *decreased* slightly in 1970 after the alleged tension ads had run (CX 822V and W). Dr. Ross testified that he could not attribute any meaning to an increase or decrease in the percentages for tension in CX 1058 and CX 1059, image studies which bracketed the period during which the Sensitive People campaign was aired (Tr. 8338, 8463-64).

781. Dr. Leavitt pretested the Leavitt Study questionnaire, CX 349, and the results of the pretest left him confident that his questionnaire was capable of eliciting tension relief responses for Bufferin and Excedrin (Tr. 6274-75), noting "it's certainly possible to get the tension or relaxation or whatever word they happen to use, that kind of response from this question" (Tr. 6278-79), especially if that attribute was salient or important to the consumer (Tr. 6279).

782. Questions six through eight in the Leavitt Study, found at CX 349X, attempted to determine the percentage of the population who felt that Bufferin and Excedrin were good for things "other than pain." (Tr. 8344). According to Dr. Ross' calculations, only 14 respondents, representing 1.8% of the total sample, stated that they thought Bufferin was good for the relief of tension (Tr. 8343). Of those 14, 11 were Bufferin users and only 3 were Bufferin nonusers as defined by the study (Tr. 8347-48). Thus, only 6/10 of 1% of the Bufferin nonusers interviewed for the Leavitt Study indicated a belief that Bufferin was good for the relief of nervous tension (Tr. 8348).

F. The Record Does Not Contain A Convincing Showing That Consumers' Beliefs About Bufferin and Excedrin Will Endure Unless Corrected

783. While the recall of specific copy points made in Bufferin and Excedrin advertising may continue for three to nine months after those claims are made, product images or beliefs about Bufferin and Excedrin can endure long after the specific information that led to their formation is forgotten (Ross, Tr. 7509-10).

784. The stability and durability of consumers' product image that Bufferin is gentler and faster acting than aspirin or that Excedrin is a more effective pain reliever than aspirin, depend on such factors as the sharpness of those images, consumers' usage of the product, the powerful principles of persuasion used in advertising that led to the formation of the beliefs, and the salience of the beliefs (Brock, Tr. 8652-60).

785. There is expert testimony that the two marketing studies in evidence (CX-346 and CX-349) provide data which show that consumers have relatively "sharp" beliefs of both Bufferin and Excedrin: most consumers have definite, as opposed to diffuse, opinions regarding the attributes of these products (Brock, Tr. 8665-67). The sharper the belief, the longer it will endure (Brock, Tr. 8652). According to Dr. Brock, analyses of these marketing studies, conducted in 1967 and late 1975, show that this "sharpness" of beliefs about Bufferin's and Excedrin's superiority has remained high and relatively unchanged for a long period of time. In Dr. Brock's view, this finding supports the conclusion that beliefs about Bufferin and Excedrin are stable and durable ones (Brock, Tr. 8665-67).

786. The beliefs that Bufferin is gentler and faster acting than aspirin and that Excedrin is a more effective pain reliever than aspirin are also salient to consumers. They stand out from beliefs about other attributes of the product's performance (CX 349; CX 346Z150, Z152; Brock, Tr. 8663-64). According to Dr. Brock, this high level of salience, as shown by the

market research studies in evidence, has remained consistently high over the time period analyzed, 1967 to 1975 (Brock, Tr. 8664).

787. The quality and consistency of salience and relative sharpness in consumer's product images of Bufferin and Excedrin suggest that they are powerful and durable (Brock, Tr. 8679). According to Dr. Brock, the fact that these beliefs have been shaped by the use of powerful principles of persuasion in advertising makes it even more likely that they will endure (Brock, Tr. 8659). Furthermore, because consumers cannot "evaluate" product differences among mild OTC analgesics, their future usage of Bufferin or Excedrin will not disabuse them of these beliefs created in substantial part by the advertising for those products.

788. Complaint counsel's expert witnesses testified that, assuming that respondents were to cease the challenged advertising claims about Bufferin and Excedrin, the product images that Bufferin is faster and gentler than aspirin and Excedrin is more effective than aspirin will persist indefinitely in the minds of consumers who use the product (Ross, Tr. 7513-14; Brock, Tr. 8698). For nonusers, Dr. Ross testified that beliefs about these attributes will endure for at least one year based upon averaging across the marketing literature which focuses upon the *sales* effects of advertising. Dr. Ross recognized that advertising's effect on images is likely to last longer than its effect on *sales* (Ross, Tr. 7513).

789. Dr. Brock testified that, because the beliefs for these attributes are high for user and nonuser alike, and are independent of experience with the product, it is reasonable to conclude that these beliefs about Bufferin and Excedrin will continue indefinitely for both users and nonusers (Brock, Tr. 8698).

790. In order to change consumer beliefs about products, a corrective message in advertising should be used (Brock, Tr. 8702; Ross, Tr. 7526-28). To increase the chances for successful communication, the corrective message should employ persuasive communication techniques similar to those used to

create the beliefs initially. It is also desirable to pre-test a corrective message before use to ensure that the corrective message is being communicated (Brock, Tr. 8705-06). Moreover, the corrective message will be more successful if the other messages in the advertisements do not contradict, conflict, or obscure the corrective message in any way (Jacoby, Tr. 9570-71).

791. Complaint counsel seek corrective advertising directed to consumer beliefs of superior efficacy with respect to Excedrin and Excedrin P.M. and superior speed and safety with respect to Bufferin. Complaint counsel do not seek any corrective advertising with respect to the tension relief images involving Bufferin and Excedrin.

792. In order to support a corrective order provision directed to the so-called establishment claims regarding efficacy or safety of the products involved, complaint counsel must show that consumers currently hold an image that:

(a) it has been established that Bufferin is faster-acting and causes stomach distress less often than aspirin;
(b) it has been established that Excedrin and Excedrin P.M. are more effective than aspirin;
(c) these images are significantly attributable to respondents' advertisements;
(d) these images have caused and are likely to cause consumers to purchase Bufferin, Excedrin or Excedrin P.M.; and
(e) these images will endure for some time after the unlawful advertisements cease in the absence of corrective messages.

793. Complaint counsel have not introduced any direct evidence concerning consumer images specified in (a) and (b) of the preceding Finding, but instead rely on inferences based on inferences: namely that it may be reasonably inferred from the inferred establishment claims regarding Bufferin, Excedrin and Excedrin P.M. that consumers currently hold corresponding establishment images about these products.

794. To the extent that the record contains evidence tending to show that consumers held superiority images about Bufferin

and Excedrin and to the extent that it may be inferred that the misleading claims alleged in Paragraphs 9 and 10 of the complaint played a significant role in creating or maintaining these images, it is found that the evidence is not so clear or convincing as to support a conclusion that these images are likely to endure for an appreciable period of time after the advertising claims have ceased.

VII. Liability Of Advertising Agencies

A. Respondent Ted Bates[7]

795. Respondent Bates actively participated in the creation and dissemination of certain of the challenged advertisements for Bufferin in its capacity as advertising agency for Bristol-Myers, commencing in February 1968 (CX 655C). That participation included development of marketing plans for the promotion and sale of Bufferin as well as creation of certain advertising themes, review of advertisements for appearance, time, position, size and reproduction (CX 655D). Bates was directly involved in the development of advertising themes including the Faster/Gentler-than-aspirin concept (CX 554A) and the "Doctors recommend Bufferin" claim (CX 560).

796. In connection with the development of Bufferin advertisements for Bristol, Bates has relied in good faith upon the judgments of Bristol-Myers' Medical Department inasmuch as Bates does not have in-house medical officers or retain medical consultants (Lanman, Tr. 11431).

797. Bates played a substantial role as Bristol-Myers' ad agency in creating and disseminating the following advertisements for Bufferin between 1968 and 1976: CX 1-7, 22-93, 95, 107, 112-114, 719-722, 751, 761R-V, Z018-020, 760R-V, Z015-016 (CX 655; CX 800). These advertisements were disseminated from 1968 to 1976 and made the representations listed in CX 815, except for Complaint Paragraphs 7A(3) and 9A(3).

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7 References to advertisements disseminated by Bates do not include CX 8-22.

798. Despite the fact that Bates created and disseminated advertisements which represented that it was established that Bufferin relieves pain faster than aspirin (Complaint ¶ 7A(1)), internal memoranda reveal that Bates knew that the comparative speed and safety claims to be open to question, although there was some scientific basis for these claims. One memorandum dated April 1969, and titled "Bufferin Briefing", stated that "clinical evidence indicates all [aspirin] work similarly well physiologically" and that all brands of aspirin were very similar in objectively proven effectiveness. It went on to add that "Bufferin cannot claim to be the best pain reliever because no one has as yet found a way of measuring time or degree of headaches relief objectively. Subjective tests have not been able to substantiate Bufferin's apparent superiority" (CX 563B, C, M; see also CX 561).

799. Bates' awareness of the limited support for the "faster" claims for Bufferin is reflected in the following comments from its files: "Everybody agrees we can't document 'best against pain' since that strongly implies relief. There's still some disagreement about being the best" (CX 556, dated 2/13/69).

800. In addition to the internal memoranda, Bates had in its files authoritative documents which specifically addressed the issue of whether faster dissolution of aspirin, and higher blood levels of aspirin, could in fact be correlated with increased or more rapid pain relief. One of these was the Food and Drug Administration's "Fact Sheet on Aspirin" (CX 469), published in November 1972. With respect to Bufferin, it stated that there was "no evidence to indicate speed of onset of its action in relieving pain is significantly increased over plain aspirin." It also concluded that certain advertising claims including the "twice as fast" claim were misleading (CX 469B).

801. Bates also had reviewed the *AMA Drug Evaluations*, Second Edition (CX 512), and expressed concern over its statement that "available evidence does not indicate that buffered aspirin tablets are preferable to plain aspirin" (CX 6468).

802. Bates knew or should have known that, at the time its advertisements were disseminated, the claims relating to comparative freedom from side effects for Bufferin were open to question. Bates had in its files, at the time the advertisements were disseminated, information which indicatsd that the claims made for gentleness had not been scientifically proven. The FDA Fact Sheet published in 1972 stated, upon comparing Bufferin with plain aspirin, that "[M]ost of the published studies indicate there is little difference in the incidence of stomach upsets after ingestion of Bufferin or plain aspirin" (CX 469B). Also, a Bristol-Myers memorandum and the accompanying Bates analysis of the second edition of the *AMA Drug Evaluation* reveals that Bates was aware of the AMA's conclusion that "results of controlled clinical studies have not conclusively demonstrated that the use of these mixtures results in . . . less gastric upset" (CX 646B). These comments, according to Bristol-Myers' own description, were the same "negative and damaging comments" which appeared in the first edition of the *AMA Drug Evaluations* (CX 646A). Furthermore, soon after Bates acquired the Bufferin account, an article appeared which was "not particularly favorable to Bufferin's medical copy" (CX 493A). That article cited findings by researchers that "people taking heavy doses of aspirin cannot protect themselves against ulcers by using buffering compounds" (CX 493B). At the very least, these findings contradicated Bates' absolute and comparative claims in the advertisements relating to side effects with Bufferin.

803. Commencing in mid-1969 and continuing through 1970, Bates disseminated a series of Bufferin advertisements which were referred to as the "Sensitive People Campaign." In an internal memorandum reviewing the status of the analgesic market information and the nature of Bufferin advertising written in April 1969, just prior to the dissemination of the advertising campaign (CX 800K-L), Bates concluded that "[T]ension is an area not currently being exploited to the degree it has been — 'Sensitive People' may exploit it" (CX 563J).

804. Furthermore, Bates' use of the "Sensitive People" advertisements to "exploit" the tension claims for Bufferin conflicted with the spirit of the NAB Code Advertising Guidelines for Non-Prescription Drugs. Emphasizing the tension relief capacity of Bufferin contradicts the NAB guide that advertising should avoid representing "that a product will alter a user's mood or attitude beyond that reasonably experienced through the relief of symptoms/conditions for which the product has been proven effective" (RX 235, Exhibit A, p. 1).

805. Documents in Bates' files reveal that Bates knew when the advertisements were disseminated that the analgesic ingredient in Bufferin was aspirin. The following comments in an internal memorandum titled "Bufferin Briefing, 4/14/69" make this clear: "Bufferin is a combination of aspirin and two antacids" (CX 563M). The memo also discusses Bufferin's place in the analgesics advertising market and what claims it can make to compete with other aspirin containing analgesics including Anacin, Bayer and Excedrin (CX 563M, N).

806. Notwithstanding Bates' knowledge that aspirin is the chief analgesic ingredient in Bufferin, Bates failed to disclose in its advertisements that Bufferin contained aspirin and suggested that the pain reliever in Bufferin was something other than aspirin. In 1969, Bates even suggested considering disclosure of Bufferin's aspirin content in advertising for the first time (CX 554M). Apparently, this suggestion was not adopted.

807. Regarding the claim that physicians recommend Bufferin more than any other OTC internal analgesic product, Bates knew or should have known that there was no reasonable basis for this claim. This fact is clearly reflected in a memorandum in Bates' files, dated April 1969, which points out that "Although doctors specify Bufferin by brand more than any other brand, they most often recommend plain aspirin" (CX 563J). This fact had been brought to Bates' attention by Walter Law, an official of CBS in charge of Program Pratices in March of 1969, who, in reviewing copy of certain advertisements, said that "doctors have no reason to specify

plain aspirin by brand name. Generic aspirin is specified 4 times more frequently than Bufferin'' (CX 560A).

808. Moreover, the supposed basis for these claims, i.e., the National Prescription Audit (CX 364-380) and the National Disease and Therapeutic Index (CX 381-390), were either invalid (NPA data represents solely prescription filling activity without considering nonprescription activity at retail pharmacies) or not supportive of the claim (NDTI showed Tylenol and generic aspirin were reommended more frequently than Bufferin) (F. 708- 09, *supra*).

B. Respondent Young & Rubicam

809. Respondent Young & Rubicam actively participated in the creation and dissemination of the challenged advertisements for Excedrin and Excedrin P.M. in its capacity as advertising agency for Bristol-Myers since before Dr. Lanman joined Bristol-Myers in 1962 (RX 1; Lanman, Tr. 11430-31). Young & Rubicam assisted its client in the creation and development of advertising strategies; creation and preparation of television and print advertisements and creation of sales promotion programs. Young & Rubicam also supervised the production of advertisements and occasionally conducted market and consumer research (CX 657). Throughout the relevant time period Young & Rubicam relied in good faith upon the judgments of Bristol-Myers' Medical Department inasmuch as Young & Rubicam did not have in-house medical officers or retain medical consultants (YRRX 231, p. 4).

810. With respect to superior efficacy claims for Excedrin, Young & Rubicam knew that there was no clearcut scientific evidence to support these claims. As late as January 9, 1970 an internal report in Young & Rubicam's files clearly stated, in a question and answer format, that ''there is no support for this claim [that Excedrin works better than aspirin] and the only explanation in laymen's terms would be the mere definition of synergism'' (CX 496A). Elaborating on the possible role of Excedrin's ingredients (i.e., aspirin, salicylamide,

acetaminophen and caffeine), the report again states that "there is no clinical efficacy story, but merely one of inference" (CX 496A).

811. In December 1970, presumably after Young & Rubicam was advised of the existence of the Emich Study (CX 425), a letter from Young & Rubicam to Bristol-Myers referring to that study stated: for "the first time ever, an OTC analgesic has been able to make the unique and distinctive claim: 'more effective'" (CX 628A). Young & Rubicam recognized the need for a high quality of scientific support for such superior efficacy claims in that same December 1970 letter, where it stated "[W]hen and if the efficacy copy is taken off the networks, we must realize that there may be great difficulty and reluctance, due to stringent network requirements, to get similar copy approved or reinstated" (CX 628A). This letter confirms that prior to the Emich Study, Young & Rubicam knew it had no adequate clinical data in support of its superior claims for Excedrin.

812. Subsequent to the Emich Study, it was not unreasonable for Young & Rubicam to have accepted the study at face value and relied on it as a reasonable substantiation for the effiacy claims for Excedrin.

813. In disseminating the claim that Excedrin is stronger and more effective than aspirin in relieving pain in certain advsrtisements for Excedrin (CX 801) and Excedrin P.M. (CX 821), Young & Rubicam represented that the ingredient giving relief was other than ordinary aspirin. In fact, Young & Rubicam impliedly represented that common aspirin was not an ingredient in Excedrin (Complaint ¶ 21). As it knew, however, aspirin was part of the Excedrin formula, it knew that this claim was false (Complaint ¶ 22).

814. With regard to tension-relief claims for Excedrin and Excedrin P.M., it is reasonable to assume that Young & Rubicam relied in good faith upon Bristol-Myers Medical Department's judgment regarding the reasonableness of scientific-medical substantiation found in general biomedical literature. Although these purported authorities were woefully outdated and did not constitute a reasonable basis for the tension

relief claim with respect to Bristol-Myers, which knew or should have known that the dated general references could no longer be relied on, at least since 1969, Young & Rubicam had no reason to question Bristol-Myers' judgment in this regard. Under the circumstancess, it was not unreasonable for Young & Rubicam to have relied on Bristol-Myers' medical judgment as to the adequacy of medical scientific substantiation for the claim.

DISCUSSION

A. The Meaning of Advertisements

It is well established that the Commission, and an administrative law judge, may determine the meaning of an advertisement solely from an examination of what is contained therein, without consumer testimony or survey data as to how an advertisement is perceived by the consumer. The test is whether, after reviewing an advertisement in its entirety, an interpretation is reasonable in light of what appears in the advertisement. An advertisement may convey more than one claim, and the same claim may be susceptible of more than one interpretation by the consumer. If an advertisement is capable of conveying more than one impression to the consumer and any one of them is false or misleading, the advertisement may be found to be false or misleading. From its own review of an advertisement, the Commission may find impressions which the advertisement is likely to convey to the public, and determine whether such impressions have a tendency or capacity to deceive the public, even in cases where a number of consumers may testify that they were not actually deceived.[8] In determining the tendency and capacity of an advertisement to mislead, the Commission looks to the impression an advertisement may make on the average consumer—the gullible and

8 *E.g., Ford Motor Company*, 87 F.T.C. 756, 794-795 (1976), and the cases cited therein.

unthinking as well as the trained and sophisticated.[9] Indeed, the central purpose of Section 5 is "to abolish the rule of *caveat emptor* which traditionally defined rights and responsibilities in the world of commerce." *FTC* v. *Sterling Drug, Inc.*, 317 F.2d 669, 674 (2d Cir. 1963).

In this connection, the unique impact of modern print or electronic commercials upon the viewer deserves further discussion. The revolutionary insight Marshall McLuhan has provided for contemporary mass communication is that "medium is the message."[10] This insight invites an understanding of the unique dimensions of today's mass-media communication. Today's printed and electronic mass communication does not aim to communicate classified data and fragments of information in the conventional sense as much as it stresses pattern recognition, in which visual and aural configurations serve as symbols. The "message" is not to be understood through the technical meaning of printed or spoken words or sounds as much as it is through recognition of the aural-visual pattern of the "medium" itself. At the risk of oversimplification, the message is recognized and understood through patterns of aural-visual symbols which are intended to evoke a desired imagery in the mind of the viewers. A casual viewer of today's television commercials is struck by the element of essential truth in McLuhan's insight. With respect to many television commercials that one encounters today, it is fair to say that their evaluation is not complete when one stops at the meaning of their technical "content"—what the spoken words say. One needs to proceed to the "pattern" of symbols—what the commercial (medium) in its totality symbolizes to the psychic and social consciousness of the audience-viewer. The key to

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9 *E.g., Charles of the Ritz Dist. Corp.* v. *FTC*, 143 F.2d 676 (2d Cir. 1944); *FTC* v. *Standard Education Society*, 302 U.S. 112, 116 (1937); *Exposition Press, Inc.* v. *FTC*, 295 F.2d 869, 872 (2d Cir. 1961), *cert. denied*, 370 U.S. 917 (1962); *National-Bakers Services* v. *FTC*, 329 F.2d 365, 367 (7th Cir. 1974); *Rodale Press, Inc.*, 71 F.T.C. 1184, 1237 (1971).

10 See Marshall McLuhan, *Understanding Media* (1964); *The Medium Is The Message* (1967).

true understanding is not literal classification and differentiation of what the viewer sees or hears, but rather the imagery evoked by the patterned aural-visual symbols.

This observation appears to have particular application to a television commercial which projects a distinct pattern of compressed, fluid pictorial and aural images, submerging its technical "content" and appealing directly to the viewer's psychic and social consciousness. In a very real sense, the viewer's critical faculties of classification and differentiation are drowned in patterns of imagery and symbols. Thus it is possible that, in skilled and practiced hands, the spoken words of a television commercial may appear to say one thing, while its pictorial and aural imagery conveys to the psyche of the viewer-audience something quite different. This observation is of some importance in evaluating many of the television commercials involved in this proceeding. For that task, wisdom of the psychology of learning is inadequate and needs to be complemented by the McLuhanian perspective. For example, this approach is especially suited to the evaluation of the television commercials involving the "tension relief" claim, which clearly depict situational tensions of various kinds that are distinguished from pain-associated tension.

In evaluating the meaning of each advertisement, I have primarily relied on my knowledge and experience to determine what impression or impressions an advertisement as a whole is likely to convey to a consumer. When my initial determination is confirmed by the expert testimony in the record, I rested. When my initial determination disagreed with that of expert testimony, I reexamined the advertisement in question, and further considered such record evidence as copy tests and verbatim responses contained therein. In any event, I have carefully considered all relevant record evidence before reaching a final determination.

The Findings regarding the meaning of advertisements as relate to the claims challenged in the Complaint are self-explanatory. However, several advertising claims challenged in the case merit further discussion.

1. The Twice As Much Pain Relief Claim For Bufferin (Complaint ¶¶ 7A(3) and 9A(3))

Complaint counsel's argument in essence is that a claim that Bufferin relieves pain twice as fast as aspirin (Complaint ¶ 7A(2)) implies a claim that Bufferin relieves twice as much pain as aspirin. However, an examination of the Bufferin advertisements cited by complaint counsel in support of this allegation (CPF 20) clearly shows that the central and simple message of these advertisements are twofold: that Bufferin acts twice as fast as aspirin and that it is gentler than aspirin. To the extent that some consumers played back the "twice as much relief" in a copy test (CX 301), it can arguably be attributed to the claim that Bufferin delivers twice as much pain reliever in the first important (or critical) minutes. However, the "twice as much relief" theme is so remote from what these advertisements can reasonably be said to convey, the verbatim evidence should be dismissed as "noise" in this instance. It follows that there is no basis for the establishment allegation set forth in Complaint ¶ 7A(3).

2. The Faster Pain Relief Claim For Excedrin (Complaint ¶¶ 7B(4) and 9B(4))

Complaint counsel's argument that a claim that Excedrin is more effective or stronger (extra-strength) than aspirin also implies a "faster pain relief" claim is unpersuasive. Most of the Excedrin advertisements complaint counsel cite (CPF 305) contain clear and simple messages that Excedrin is an extra-strength pain reliever, that it acts fast and lasts longer. However, a number of Excedrin advertisements did contain "*faster* pain relief" claim, either expressly or impliedly. E.g., CX 115, 135, 145, 146. And, a comparative claim also implies an establishment claim, for the reasons discussed hereinafter.

3. *The Tension Relief Claims For Bufferin, Excedrin and Excedrin P.M. (Complaint 12A and B)*

A number of Bufferin commercials contain an implied claim that Bufferin is also an effective reliever of tension, with or without headache pain, and thus enables persons to cope with the ordinary stresses of everyday life They include: CX 715, 49-60. While the verbal messages in these advertisements contain the words "headache pain," the overall impression one gets from each of these advertisements is unmistakably that Bufferin is good for tension, with or without headache pain, and generally good for tense situations one encounters in everyday life. Indeed, the impact of the visual presentation is so dominant in these TV commercials that any passing reference made to headache pain is entirely submerged, even when one looks at the storyboards with the verbal messages spelled out in print.

A number of Excedrin commercials contain express or implied claims that Excedrin is a good tension reliever. They include: CX 115-116, 120, 121, 124-125, 127-128, 132-133, 135-139, 141-144, 148, 150, 183. Many of them contain clear and direct verbal and pictorial claims that Excedrin has a "tension reliever" and "an anti-depressant" in addition to a pain reliever--as direct and explicit a tension relief claim as any that can be devised.

Two Excedrin P.M. commercials contain an implied claim that Excedrin P.M. is good for tension relief, especially at night time, with or without pain. They are CX 216 and 219. The other ads complaint counsel cite in CPF 369 present a close question. It is of course arguable that these too contain an implied claim of general tension relief at night time. However, the overall impression of these short ads is unmistakably that the "relaxing" claim is clearly related to a "sleep aid" claim. They are a world apart from the tension relief advertisements reviewed above for Bufferin and Excedrin. As to the remainder of advertisements cited in CPF 369, therefore, I am unable to find an implied general tension claim. The copy test evidence cited in CPF 370 and 375 is not persuasive in these

circumstances. In my view, it simply reflects the fact that a mere mention of the word "relax" in any context is likely to evoke in the mind of some consumers an association with general tension. The Excedrin P.M. advertisements should not be indiscriminately condemned for that reason.

4. *Claims Related To Ingredients (Complaint 21)*

(a) *The Claim That The Pain Reliever In Bufferin Is Something Other Than Aspirin*

Numerous advertisements for Bufferin contain an implied claim that the pain relieving ingredient or pain reliever in Bufferin is something other than aspirin. Every Bufferin advertisement that refers to faster pain relief or gentleness implies that Bufferin's pain relieving ingredient is not aspirin. In my view, this claim, although not expressly made, is an insidious one and comes through very clearly in these advertisements. These advertisements include all Bufferin advertisements which are listed in Column 14 of CX 816. The fact that the advertisement frequently compares Bufferin with "plain" or "simple" aspirin does not alter the conclusion that most consumers will perceive the comparison to be Bufferin v. aspirin.

(b) *The Claims That The Pain Reliever In Excedrin Is Something Other Than Aspirin and That The Anti-Depressant In Excedrin Is Something Other Than Caffeine*

Numerous advertisements for Excedrin contain an implied yet clear claim that the ingredient that gives longer lasting pain relief or extra-strength pain relief in Excedrin is not aspirin and the anti-depressant contained in Excedrin is not caffeine. They include: CX 115-116, 122-139, 141-167, 169-173, 175-186, 188-191, 193, 202-211. CX 115 and 116 are good examples. A viewing of the TV commercials will persuade the most skeptical. Although the chemical formulas a viewer sees on the screen are in fact true, they are not likely to mean any-

thing to an average viewer but that the long lasting pain reliever in Excedrin is different from aspirin and that the anti-depressant that restores one's spirit in Excedrin is different from caffeine. Furthermore, a number of Excedrin advertisements which feature the "Excedrin Headache" theme impliedly claim that the pain reliever in Excedrin is special, stronger, and unlike aspirin. They include CX 122-139, 141-152.

5. *The Establishment Claims (Complaint ¶ 7))*

While a few advertisements in evidence contain an *express* statement that medical research in hospitals and clinics "have established" a proposition (*e.g.*, CX 100, 101), most of the advertisements in evidence do not contain the word "established." The record as a whole shows that the word "established" is not a word commonly used or understood by average consumers. However, the record shows that "established" is not an uncommon term in the biomedical sciences. Also there appears to be a general agreement among clinical pharmacologists and researchers that the term may be used loosely to mean that a study "shows" or "demonstrates" a proposition, or in a narrow, technical sense to mean that a proposition has been scientifically proven or accepted as true by the community of trained and qualified scientists and researchers, based on well-controlled clinical studies. In formal statements filed with the Federal Trade Commission in 1967 and 1968 in connection with a proposed Trade Regulation proceeding involving nonprescription analgesic products, Bristol-Myers used the term "established" in the narrow, technical sense and asserted that superiority of one analgesic product over another is not "established" unless based on a number of clinical pain studies demonstrating such superiority (Tr. 12023-24; CX 908, p. 31; CX 907, p. 14). And a number of complaint counsel's expert witnesses testified to their understanding of the word "established" in a similar, technical sense.

Secondly, a number of advertisements for Bufferin and Excedrin claiming superior speed, efficacy or safety made *ex-*

press references to medical-scientific evidence, such as hospital studies, clinical studies, blood level studies, chemical formulas, anatomical models and graphs. See *e.g.*, Bufferin advertisements: CX 2-4, 7, 10, 13, 34, 61-64, 67, 91- 96, 98-101, 113-114, 721; Excedrin advertisements: CX 115-116, 118-121, 124-125, 132-133, 138-142, 144, 153-161, 164-167, 170-171, 173, 175-177, 182, 184-185, 202-204, 208, 736. CX 99, a Bufferin print advertisement, displaying a picture of anatomical model and a blood level graph comparing Bufferin and "aspirin," suggests that "Clinical studies prove" (bold types) that Bufferin acts twice as fast as "aspirin" to relieve pain.

Thirdly, there is uncontradicted expert testimony in the record that when consumers see an advertisement containing a scientific or pharmacological claim, they assume that there is a valid scientific basis for that claim and that such a claim would not be permitted by the authorities unless there was a valid scientific evidence to prove it (Ross, Tr. 7024, 7026, 7036).

Finally, the rationale of the Commission's reasonable basis requirement, as articulated in *Pfizer*,[11] compels a conclusion in the circumstances of this case that, as a matter of marketplace fairness, a superiority claim regarding Bufferin, Excedrin and Excedrin P.M., without more, implies a representation that the claimed superiority, in terms of speed of action, effectiveness or gentleness, has been sufficiently demonstrated by medical-scientific evidence, namely, estsblished.

For all of the foregoing reasons, it is concluded that every advertisement for Bufferin, Excedrin, or Excedrin P.M. which was found to contain a comparative claim as alleged in Paragraph 9 of the Complaint also made the establishment representations alleged in the corresponding subparagraphs of Paragraph 7 of the Complaint.

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11 *Pfizer, Inc.*, 81 F.T.C. 23 (1972).

B. Pain

Pain is said to be the most common symptom for which man seeks relief by medication. It is generally agreed that mild to moderate pain that is self-limited (''minor pain'') may be treated symptomatically by self-medication.[12] Pain is a subjective condition of diverse and often obscure etiology and defies a precise definition. Beecher, a recognized authority in the study of pain and analgesia, has observed that:

> Pain is a subjective matter clearly ''known to us by experience and described by illustration.'' [However,] lexicographers, philosophers and scientists have none of them succeeded in defining pain. Having said that it is the opposite of pleasure, or that it is different from other sensations (touch, pressure, heat, cold) or how it is mediated (through separate nerve structures), or what the kinds of it are (bright, dull, aching, pricking, cutting, burning), or what kinds of things will produce it (trauma to nerve endings or to nerves, electric shocks, intense stimulation of the sensations of touch, pressure, heat, cold), or what it comes from (injury, bodily derangements, or disease), or that certain types of mild stimulation can probably be stepped up to a painful level through conditioning or what some reaction patterns to it are (escape or avoidance), none of these individual statements, nor indeed their sum total, provides a definition of pain.[13]

''Minor pain'' was defined by the FDA OTC Internal Analgesics Panel as ''pain that is self-limited and which requires no special treatment or prior diagnosis by a physician.'' Minor pain is usually described as pain ''of mild to moderate intensity as opposed to sharp, severe and/or protracted pain.''[14]

12 CX 514, at 35350.

13 CX 514, at 35350-51.

14 CX 514, at 35351.

C. Aspirin and Aspirin Products

It is not surprising that aspirin is by far the most widely used OTC drug in the United States. It is estimated that almost 19 billion dosage units are sold annually. Since aspirin was introduced into the American market 80 years ago, it has been discussed extensively in the medical-scientific literature.

Although such important aspects of aspirin's pharmacological profile as the specific mechanism of its action and the localization of the site of its chemical action in humans are yet to be definitively determined, a considerable amount of biopharmacologial data has been published with respect to the relationship between the dosage of aspirin and its analgesic action and the mechanism of its metabolism in animals and humans. It is now generally agreed, primarily on the basis of historial data, that aspirin is safe and effective as a mild analgesic, antipyretic and antirheumatic agent for humans.

It is generally believed that aspirin alleviates pain by both a peripheral effect (i.e., blockage of pain impulse generation) and a central nervous system (CNS) effect.[15]

Aspirin is also an effective antipyretic or fever reducer, and may be safely used for self-medication when fever is due to the common cold or flu. Aspirin lowers the temperature in patients with fever but has no effect on the body temperature when it is normal. Heat loss is increased by increased peripheral blood flow and sweating, which is caused by a central action of aspirin on the hypothalamus.[16]

Inflammation and many rheumatic diseases often are accompanied by pain and sometimes fever. Since in many rheumatic conditions the object of therapy is to stop the disease process which usually requires drug dosages higher than those recommended for OTC use, OTC drugs for the treatment of inflammatory conditions and rheumatic disease should be used only under the advice and supervision of a physician. Aspirin

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15 CX 514, p. 35351 at 35381.

16 CX 514, at 35351-52.

acts as an agent which reduces joint or muscle tenderness or swelling. The precise mechanism or mechanisms of action by which aspirin produces anti-inflammatory effects is not known.[17]

As a result of the remarkable progress in biomedical sciences during the recent decades, the knowledge and understanding of aspirin's other biological effects have been substantially expanded, promising both new benefits (such as the use of aspirin in anticoagulant therapy) and risks (such as the problem of aspirin intolerance). Based upon an exhaustive review of available data in biomedical literature, the FDA OTC Internal Analgesics Panel concluded in 1977 that the most appropriate label indications for pain for OTC analgesic agents including aspirin should state: "For the temporary relief of occasional minor aches, pains and headache." It is generally agreed that aspirin is effective in mild to moderate pain although of limited value in severe pain. Recurrent or chronic pain, even of minor intensity, such as frequent headaches or joint pain which flares up periodically, may indicate pathologic condition and should not be treated with OTC analgesics except under the advice and supervision of a physician.[18]

Since one of the most prevalent uses of aspirin and aspirin-containing products is in the treatment of headache pain, it is important to have a general understanding of this all too common affliction.

D. Headache Pain

Headache, or cephalalgia, is a unique symptom and an ambiguous term for pain having many different etiologies. The most common type of headache is occasional headache, which is transient (usually lasting less than one day) and may be secondary to many factors including fatigue, tension, eyestrain,

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17 CX 514, at 35352.

18 Generally see CX 514 at 35351, 35381-83; Stevenson, Tr. 1481-88; Farr, Tr. 2566-70.

fever or alcohol ingestion. The chronic or recurrent headache may be caused by more serious underlying diseases such as vascular disturbances, brain tumor or abscess, intracranial lesions or lesions of the eye, nose, ear or throat.[19]

Headaches can be differentiated into three major categories: vascular, psychogenic and traction-inflammatory headaches. Vascular headache is provoked by the tendency for vasodilation that accompanies physiological changes in cranial blood vessels. Common types of vascular headaches are hypertensive, migraine and toxic. OTC analgesics are inappropriate for hypertensive or migraine headaches. Psychogenic headache, one of the most common types of headache, accounts for up to 90% of chronic headaches. It is accompanied by persistent contraction of the muscles of the head, neck, and face, and may even be described as a sense of pressure rather than a true pain. Apprehension, anxiety, post-traumatic experiences and depression, as well as the individual's life stresses and habits, can precipitate the symptoms. Psychogenic headaches are often described by synonymous terms such as muscle contraction and tension headache. Self-medication using OTC analgesic drugs is generally contraindicated for chronic psychogenic headache. Traction and inflammatory headache, evoked by organic disease, is associated with inflammatory disease of the meninges, and intracranial or extracranial arteries or phlebitis. Although the FDA OTC Internal Analgesics Panel concluded that the occasional headache is self-limited and requires no medication, it recognized OTC analgesics' usefulness for symptomatic treatment.[20]

E. Complaint Counsel's Burden of Proof

The Complaint in this proceeding essentially challenges certain simple or comparative efficacy and safety claims regarding Bristol-Myers' three OTC analgesic products, Bufferin, Excedrin and Excedrin P.M., and alleges that these advertising claims have not been established or did not have a reason-

19 CX 514 at 35352.

20 CX 514 at 35353.

able basis. With respect to Bufferin, the core fact issues are (1) whether Bufferin's faster-pain-relief claim has been established, (2) whether Bufferin's fewer-stomach-upset claim has been established, and (3) whether Bufferin's tension relief claim had a reasonable basis. With respect to Excedrin, the core fact issues are (1) whether Excedrin's superior efficacy claims have been established, and (2) whether Excedrin's tension relief claim had a reasonable basis. With respect to Excedrin P.M., the core fact issues are (1) whether Excedrin P.M.'s superior and unique (night time pain relief) efficacy claims have been established. With respect to each of these fact issues, complaint counsel have the burden of proving by a preponderance of credible evidence that the challenged advertising claims have not been established or did not have a reasonable basis.

Complaint counsel have attempted successfully, in my view, to discharge that burden by showing that these biomedical propositions have not been scientifically demonstrated by two or more well-controlled clinical studies, or (with respect to noncomparative claims) that the propositions did not have a reasonable basis in biomedical sciences. On the other hand, respondent largely relied on failure of proof on complaint counsel's part and sought to show, by clinical and experimental pain studies, expert testimony and references to biomedical literature, that the challenged superiority claims have been established by well-controlled pain studies or serum salicylate concentration studies, that the superiority claims have been

generally accepted as valid by the medical-scientific community and that the noncomparative claims had a reasonable basis in scientific facts.[21]

Accordingly, the resolution of the core fact issues outlined above necessitated an evaluation of rather complex and technical biomedical and statistical evidence presented by the parties, with the aid of expert testimony. However, since clinical pharmacology and medicine are not exact sciences, especially when, as here, dealing with such subjective matters as pain and subjective response, a resort to common sense was necessary.

F. Well Controlled Human Studies Are Required In Order To Establish A Biomedical Proposition Regarding the Efficacy or Safety of A Drug

The record as a whole clearly shows that, at least since the early 1960's, in order to establish a biomedical proposition regarding the efficacy and safety of drugs in man, well-controlled human clinical studies showing statistical significance are required as a rule, by the medical-scientific community as well as by learned journals and the FDA.

The expert testimony, corroborated by the 1977 final report of the FOA OTC Analagesics Panel, shows that the essential

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21 A brief general comment from a lay perspective may be in order here with respect to Bristol-Myers' suggestion that no biomedical proposition regarding absolute or comparative efficacy or safety of drugs can be established in the sense of being conclusively proven by objective facts. Apart from epistemological considerations, it is true that the biomedical science is not an "exact" science and that comparative analgesiology is essentially based on a subjective methodology (the subjective pain response model). However, to the extent the biomedical science subscribes to the scientific method of hypothesis testing and statistical analysis, we are not free to bend or modify the concomitant rigors of that method in search of a desired conclusion. For example, a bioassay either shows a statistically significant difference between Excedrin and aspirin, or it does not. Where a bioassay fails to produce a statistically significant difference between Excedrin and aspirin at the conventional 95% level with acceptable confidence intervals, that negative result should be acknowledged for that bioassay with scientific humility; it should not be transformed into Excedrin's "superiority" by statistical or computer manipulations of the same data.

criteria for a well-controlled clinical study include the following: (see F. 366, supra):

(1) The study should be double blinded;

(2) A protocol should be prepared before a study begins and be adhered to throughout the study;

(3) Test subjects should be randomly assigned to treatment groups;

(4) A placebo control is preferred wherever practicable;

(5) The investigator must be unbiased and experienced;

(6) Appropriate statistical methods contemplated in the protocol should be used to evaluate the data.

The above requirements with respect to a well-controlled clinical demonstration are not a product of the whim of a handful of partisan pharmacologists. On the contrary, they represent a crystallization of slow and deliberate evolution in the development of a scientific method in clinical pharmacology that began in the early 1950's. By the early 1960's, clinical pharmacologists, including respondents' medical-scientific experts, lived by them. Any learned journal of any consequence would not accept for publication a clinical trial of therapeutic agents which purports to measure their efficacy unless the study satisfies all of the essential elements of those requirements. Indeed, since the advent of the 1962 Amendment to the Food, Drug and Cosmetic Act, the FDA has incorporated these requirements into its regulations governing new drug applications for both prescription and nonprescription drugs.[22]

Pursuant to the FDA's specific mandate, the FDA's OTC Analgesics Panel set forth the criteria for well-controlled studies which OTC analgesic products must meet in order to estab-

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22 21 C.F.R. § 314.111(a)(5)(ii)(a) through (c) and § 330.10(a)(4)(ii). In the words of the FDA, the principles underlying these requirements

> have been developed over a period of years and are *recognized by the scientific community as the essentials of adequate and well-controlled clinical investigations*. They provide the basis for the determination whether there is "substantial evidence" to support the claims of effectiveness for "new drugs. . . ." (21 C.F.R. § 314.111(a)(5)(ii)) (Emphasis added).

lish efficacy. They are virtually the same as those the expert witnesses in this processing specified. Specifically, to "establish Category I status for a Category III compound,"[23] the Panel required "at least two studies by independent investigators" (CX 514 at 35445) which conformed to the following criteria:

> (1) Allocation of subjects to treatment groups should be done in such a way as to avoid bias;
> (2) The double-blind technique should be used;
> (3) The randomization procedure should balance out the variables not otherwise controlled in the patient selection;
> (4) Suitable controls should be used, including graded doses of an analgesic standard and possibly a placebo as well;
> (5) The scoring of pain and relief should be done frequently;
> (6) Prior to carrying out an analgesic assay, the appropriate statistical analysis should be be defined. (CX 514 at 35444-45).

Unless these requirements were satisfied, the Panel concluded, "any statistical analysis would only impart a false sense of confidence in the results," (CX 514 at 35445).

Respondents' expert witnesses do not dispute the essential validity of the scientific rationale for these requirements, including the principle of replication. Drs. Lanman and Elvers, Bristol-Myers' Medical Director and Associate Medical Director respectively, are in a position to appreciate the practical importance of these requirements with respect to the OTC analgesic products Bristol-Myers markets. And, in my view, the

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23 Three "categories" - Category I, II and III — were used by the FDA Analgesics Panel, as well as all other OTC drug panels. Category I was defined as "generally recognized as safe and effective." Category II was defined as "not generally recognized as safe and effective." And Category III was defined as "[c]onditions for which the available data are insufficient to permit final classification [*i.e.*, Category I or II] at this time." (CX 514 at 35348).

importance of these requirements increases when the question becomes one of comparative efficacy or safety rather than simple efficacy or safety.[24]

G. Excedrin's Superior Efficacy Claim Has Not Been Established

In my view, complaint counsel have discharged their burden with respect to Excedrin's superior efficacy claims. The record as a whole shows that Excedrin's superior efficacy claims have not been established by well-controlled clinical studies using appropriate subjects. Bristol-Myers attempted to rebut complaint counsel's *prima facie* showing essentially by: (1) showing that the two bioassays conducted for the purpose of determining relative potency estimates of Excedrin as against aspirin (the Emich Study, CX 425, and the Smith Study, CX 453), are well-controlled clinical studies which establish Excedrin's superior efficacy for pain of all types; (2) showing that the experimental study of electric-shock induced dental pulp pain study (the Sherman Study, CX 439) comparing threshold pain elevation effects of Excedrin and aspirin, was a well-controlled study supporting Excedrin's superior efficacy; (3) by showing that, on a pooled basis or on the basis of nonparametric analysis, the two relative potency studies establish Excedrin's superior efficacy; and finally by several references to what relative potency studies purport to show about comparative performance of analgesic products.

1. *The Emich Study (CX 425)*

The 1968 Emich Study (CX 425) was a bioassay which compared three graded doses (1, 2 and 4 tablets) of Excedrin,

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24 In fact, the FDA OTC Analgesics Panel discussed comparative efficacy issues on a number of occasions. For example, it provided the Category III "faster to the bloodstream" claim for buffered aspirin could be moved to Category I only if clinical studies demonstrated that buffered aspirin provided quantitatively faster analgesia than aspirin (CX 514 at 35480-81). Likewise, the Panel determined that caffeine could be moved to Category I as an adjuvant only if it could be demonstrated that caffeine provided a "statistically significant contribution to the total effect" of 650 mg. aspirin, *i.e.*, that it meaningfully enhanced the analgesia provided by 650 mg. aspirin (CX 514 at 35445).

5-grain (about 325 mg.) aspirin and placebo, using female patients with post-partum pain and found elative potency estimates (rho) of 2.27 to 7, depending on the variables used for analysis. However, by conventional variables analysis, only one (based on SPID 5 analysis) of the four rejected the null hypothesis of equipotency (rho of 4.08, with a 95% confidence interval of 1.3 to 3.84 x 10^{24}). That is, only one analysis shows a statistically significant difference between Excedrin and aspirin at the 95% level of confidence (F. 484). Taking into account the *post hoc* adjustment (% SPID) and additional variables analyses increases that number to three out of six. From this, Bristol-Myers argues that the Emich Study supports Excedrin's superiority to aspirin.

The Emich Study's conclusions, however, are clouded by a serious problem of baseline pain imbalance. Apparently after randomization procedure was followed, more severe pain subjects ended up in the Excedrin treatment groups than in the aspirin groups, thus increasing Excedrin's chances of showing greater pain relief compared to aspirin. Baseline pain imbalance is obviously a fundamental problem, involving as it does the most important variable in a bioassay, and can render the entire study questionable. The investigators in CX 425 used % SPID method in an attempt to adjust or correct the baseline pain imbalance. However, the record as a whole clearly shows that this method, although arguably a statistically defensible procedure, cannot be expected to remove entirely the shadow cast by the baseline pain imbalance and is rarely used in analgesic bioassays,[25] for the simple reason that baseline pain is

25 Apparently only one analgesic study has been published in biomedical literature that reported statistically significant dfferences in baseline pain levels among the treatment groups (Tr. 10626-27). In that study, Dr. Louis Lasagna, an eminent clinical pharmacologist, determined that, because of the bias introduced by baseline pain imbalance, he could not come to conclusions about the performance of the tested drugs (Tr. 5903, 9721, 10626-27). Dr. Forrest could not remember any published study which had such imbalances (Tr. 8962).

perhaps the most important variable in a pain study.[26]

In similar circumstances, Dr. Forrest would have started all over again, although he would not have discarded the Emich data entirely. Dr. Brown testified that, although he would not say that the Emich Study was invalid from a methodological point of view, he did not know what to make of the Emich data and that he could not draw any firm conclusions from the Emich Study.

Therefore, the Emich Study (CX 425) does not provide a scientific basis for any firm conclusions regarding Excedrin's therapeutic superiority over aspirin, although it generated some interesting data suggesting the need for further study.

Finally, Bristol-Myers' argument that the requirement for 95% confidence level in analgesic bioassays is not appropriate is rejected. In my view, when the claim involves superior efficacy (not simple efficacy or lack of it), the confidence level becomes more critical and certainly it should not be relaxed. The fact is that the multiple analysis of the same data through a computer model using six variables produced three relative potency estimates that are not significantly different from 1.00 (SPID 4, Total 4 and Total 5).[27]

2. *The Smith Study (CX 453)*

The Smith Study which commenced in 1970 is a bioassay comparing three graded doses (1, 2 and 4 tablets) of Excedrin,

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26 Also, from a layman's perspective, the basic objection to baseline pain imbalance in a bioassay of pain relieving drugs is that the study is loaded in favor of one drug. This objection is not satisfied by the suggestion that the problem may have been due to pure chance and that the investigators were not biased in patient assignment to treatment groups.

27 Again from a layman's perspective, the fact that a comparative pain relief study can show a statistically significant difference in favor of Excedrin for some study variables but not for others is not persuasive that Excedrin has a real, meaningful difference. What a consumer expects from a headache tablet claimed to be stronger and more effective than aspirin is not a technical, now-you-see-now-you-don't difference, but a clearcut superiority demonstrated by definitive studies that are beyond question and accepted by the biomedical scientific community as valid. This observation applies to all pain studies in the record.

325 mg. aspirin and placebo, using female patients with postpartum pain at the Boston Hospital for Women, under the direction of Dr. Eugene Smith, a reputable clinical pharmacologist. There is evidence tending to show that the Smith Study was intended to be a long-term study, funded by Bristol-Myers, for the purpose of estimating the relative potency ratio of Excedrin to aspirin and also of exploring the relative importance of major variables among test subjects. In any event, CX 453, referred to as the Smith Study in this proceeding, is a report based on the data generated from the fall of 1970 through January 1972, which was prepared by Dr. Smith and transmitted to Bristol-Myers.

CX 453 was a well-controlled study. The sample size (about 785) was unusually large, thus increasing the reliability of the results. All variables which could have exerted an influence on the treatment groups were balanced (Smith, Tr. 5434, 5506-07). The Smith Study showed consistent results by all analysis. All of the analyses favored Excedrin over aspirin, but none of them showed a statistically significant relative potency ratio with a 95% confidence interval above 1. See F. 506-08.

In every respect, the Smith Study is preferable to the Emich Study in terms of reliability, and its negative findings darken the shadow over the Emich Study discussed hereinabove.

3. *Pooled Analysis of Emich and Smith Studies*

Bristol-Myers' argument that an examination of the Emich and Smith Studies (CX 425 and 453) on a pooled basis sufficiently demonstrates Excedrin's superior efficacy is not persuasive. To begin with, Bristol-Myers' reliance on pooled analysis of the Emich/Smith data is inconsistent with its position that CX 453 is an interim report of an uncompleted study. Furthermore, the pooling of the two studies is subject to a basic objection that the two studies are not comparable and should not be pooled. The situation here is sharply distinguishable from a cooperative project, where the data generated at different hospitals by different investigators under a single protocol are pooled for a uniform and overall analysis. Although it is arguable that the "pooling" procedure employed *post hoc* by

Dr. Laska here may be statistically defensible, the proposition that a combination of two studies, each of which is incapable of showing a statistically significant difference by itself, can through "pooling" produce a statistically significant difference is difficult to accept for a layman. Indeed, there would seem to be little logic in piling up negative results and hoping to come up with an affirmative conclusion. Although Bristol-Myers' argument for "pooling" has some statistical plausibility, it is just as plausible, if not more so, to argue that the pooled results in the record as a whole fail to show a statistically significant difference between Excedrin and aspirin.

Dr. Brown was also emphatic that biomedical researchers do not engage in multiple analyses of the same data in search of statistical significance (Tr. 5014). *Post hoc* data massaging, regardless of whether through multiple analyses or pooling, only imparts a false sense of confidence and may end in misleading or distorted results. Such procedures should not be relied on as establishing or sufficiently demonstrating a superior efficacy claim.

4. *The Sherman Study (CX 439)*

The Sherman Study (CX 439), entitled "Comparison of the Effectiveness of Two Analgesic Agents by Laboratory Testing," is the report of a 1962 study of electric-shock induced dental pulp pain, comparing the threshold elevation effects of 2 tablets each of Excedrin and aspirin. The Sherman Study reported that in 65 tests on 14 subjects, Excedrin caused an average pain threshold elevation of 15%, and in 48 tests on 15 subjects aspirin caused an average pain threshold elevation of 2.7%, and concluded that Excedrin is more effective than aspirin in elevating the pain threshold to electrical stimulation to the dental tooth pulp.

The basic problem with the Sherman Study is that, until a few years ago, there was a general agreement among clinical pharmacologists who studied analgesic agents that pain threshold elevation studies of experimental pain (as distinguished from subjective response studies of clinical or pathological pain) are not reliable predictors of the analgesic performance

of a drug for clinical pain in man. Although such a renowned clinical pharmacologist as Dr. Beecher of late has begun to take another look at the pain threshold studies *in conjunction with* bioassays, the prevailing view among clinical pharmacologists remains to be that the usefulness of an electric shock induced dental pulp pain study by itself as a reliable predictor of competitive performance of analgesic agents is seriously limited.[28]

5. *Relative Potency Studies and Comparative Efficacy of Excedrin and Aspirin*

The concept of dose-response relationship is a pharmacological formulation of the common sense notion that there is a relationship between the amount of drug and the intensity of the drug's biologic effect. The dose-response studies are attempts to quantitate this relationship and are usually expressed graphically, by way of dose-response curves. Thus, the dose-response curve is a graphic expression of the drug's anticipated intensity of action at various dose levels and must be interpreted in terms of such variables as the weight of test subjects, the ratio of the rate of absorption and distribution to the rate of detoxication or excretion, the physical properties of the drug and other specific characteristics of the test subjects. On the other hand, because of the peculiarities of individuals, judgment factors are inevitably involved. The subjective pain response studies using the bioassay technique are attempts to apply this concept to natural or spontaneous pain states.

A relative potency study is a bioassay of graded doses of a standard drug and a test drug for the purpose of estimating the relative potency ratio of the test drug to the standard, from dose-response curves of the standard and test drugs. As such, its product, the relative potency estimate, is generally accepted as a useful statistical ratio in gauging the appropriate

28 In addition, the Sherman Study appears to have suffered from a number of methodological problems. See F. 554-58, *supra*. Also, the authors of CX 439 were at the time careful to limit the applicability of the threshold elevation effects to dental pain or other pain that is transmitted through pathways similar to that of dental pulp pain. The record is not clear whether headache pain, for example, is transmitted through the same pathways as dental tooth pulp pain (F. 550).

dose of the test drug for a given dose of the standard drug (a dose-finding function). Before a relative potency estimate thus derived can be valid, certain underlying assumptions must be shown to be true. They include: (1) the assumption of linearity of the dose-response curves; (2) the assumption of parallel dose-response curves; and (3) the assumption of equianalgesic range.

Thus, the primary purpose of a relative potency bioassay of analgesic drugs is to produce a best relative potency estimate of the test analgesic drug to the standard analgesic drug across the dose ranges: It is not to compare their analgesic effectiveness at any specific dose level or to determine the magnitude of the differences, if any. Therefore, relative potency estimates can be misleading when used as an indicator of comparative efficacy of two drugs at specific doses. For example, when the slope of the dose-response curves is shallow or almost flat, the two drugs may be equally effective for all practical purposes in spite of a relative potency estimate indicating significant difference. The reason is simply that when the parallel dose response curves are shallow, one would find little difference in the effect for an incremental increase in dose, and a large increase in dose is required to obtain a relatively small increase in effect.[29] On the other hand, when the slope of the dose-response curves is steep, assuming identical relative potency estimate as in the example given above, an incremental increase in dose will produce a markedly increased effect. When the results of a relative potency study using bioassays are to be used for the purpose of estimating the comparative efficacy of the two drugs at a specific dose level, it is essential that (1) the best relative potency estimate (rho) be statistically significant at the 95% confidence level *and* (2) the confidence intervals do not enclose 1. Otherwise it cannot be concluded that there is a statistically significant difference in *effectiveness* between the two drugs at a given dose level. Generally see F. 418-35.

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29 See CX 514 at 35364.

For all of the foregoing reasons, Bristol-Myers' arguments that bioassay data can be looked at anyway one chooses, that the rigid 95% confidence level is inappropriate in the context of this proceeding, and that pooled analyses of all available bioassay data favoring greater efficacy of Excedrin over aspirin provide adequate demonstration of Excedrin's superior efficacy must be rejected as unpersuasive.

6. *The Excedrin Formulation*

Bristol-Myers' argument that Excedrin contains larger amounts of analgesic and therefore is more effective than aspirin is rejected. Excedrin's analgesic ingredients (aspirin, acetaminophen and salicylamide) amount to 65 grains, compared to 5 grain aspirin. In addition, Excedrin contains caffeine. The record as a whole clearly shows that the proposition "more is better" has no basis in clinical pharmacology as far as mild OTC analgesic products are concerned. And, caffeine's effectiveness as as analgesic adjuvant has not been adequately demonstrated. The three blood level studies introduced by Bristol-Myers (the Booy, Wojcicki, and Dahanukar Studies) are of little value. The Houde and Wallenstein Studies are equivocal and inconclusive by the authors' own characterization. Indeed, it is arguable that Excedrin contains a smaller amount of proven analgesic ingredients than a 5 grain aspirin tablet.

7. *Is All Pain Alike?*

Bristol-Myers' reliance on clinical studies using post-partum pain in this case implicitly assumes that all pain is alike, that what is shown with respect to post-partum pain can be assumed to be true with respect to all types of pain, regardless of particular etiology involved. However, the record strongly suggests that this assumption may not be valid and needs to be demonstrated.

For some years, clinial pharmacologists and researchers have assumed uncritically that if a drug is shown to be effective for the relief of one type of pain it will be effective for other types of pain as well. This convenient assumption is cer-

tainly understandable in view of the fact that for many years the researchers in this field have been preoccupied with attempts to develop a satisfactory methodology for measuring analgesic performance. However, the fact that they did not study mixed pain subjects in a study in spite of the fact that patient availability and acessibility often presented major problems, bespeaks their implicit recognition that pain of diverse etiology should not be commingled in a single study. In any event over the years they have come to recognize that some types of pain responds differently to an analgesic drug. Well known examples are migraine headache, uterine cramp pain, and pain accompanied by inflammation. As a result, an increasing number of clinical pharmacologists and researchers, and the FDA, are coming around to the position that at least one study should be done with the type of pain for which the drug is to be used. See F. 379, *supra*.[30] However, there appear to be respected clinical pharmacologists who do not support this conservative proposition: They would wait for the day when the contrary proposition (all pain is not alike) is demonstrated by consistence evidence.[31]

The bioassays and experimental pain studies Bristol-Myers relies on in this proceeding do not address the issue of Excedrin's superior efficacy for the relief of headache pain.

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30 The FDA OTC Analgesic Panel shares this view. In discussing Category III combination products, the Panel states that the clinical test should be related to the symptoms for which the combination is designated. CX 514 at 35371. The NAS/NRC Analgesic Review Committee's recommendations during the 1960's that if an analgesic drug has been shown to be effective in one or two kinds of pain the drug be certified as a general purpose analgesic product in the absence of contrary evidence is often cited as authority for the all-pain-is-alike dogma. The Committee's recommendation was undoubtedly a sound expedience in the massive drug screening project for which the Committee labored long and hard, where the concern was whether a product was an effective analgesic drug, and not whether a product was a more effective analgesic drug than another product for designated conditions. However, that expedience cannot be transformed into a universal scientific proposition that clinical study findings of cancer pain, post-partum pain and post-operative pain apply egually to headache pain or other minor pain. (Tr. 12187; CX 511 H).

31 From a layman's perspective, the proposition that all pain is alike does not accord with our common experience. Any experienced person will agree that headache is not like post-partum pain or dental pain.

Bristol-Myers' witnesses agreed that headache pain studies can be done, although they are more difficult than other pain studies. In my view, *the importance of the question whether all pain is alike increases when the issue is comparative efficacy for designated conditions rather than simple efficacy or lack of it.*

8. *Excedrin and Aspirin May Be Equally Effective For The Relief of Mild Pain*

Finally, none of the studies Bristol-Myers relies on specifically addressed the question of Excedrin's superior efficacy over aspirin for the relief of mild pain. Since OTC analgesic products are indicated for the relief of mild pain, relative potency studies and relative potency estimates are meaningless unless they are shown to be valid for mild pain. The only evidence bearing on this question in the record is the testimony of Drs. Sunshine and Laska regarding what the Emich and Smith data can show with respect to the mild and moderate pain subgroups. (Tr. 9837-40) However, the Emich and Smith studies fail to show statistically significant difference between Excedrin and aspirin for the relief of mild to moderate pain. *First*, the Emich study excluded all mild pain subjects, and the number of moderate pain subjects was too small (less than 15) to provide any meaningful results. *Second*, the number of mild pain subjects in the Smith study was too small to provide statistically significant results, although the Smith study's overall sample size (785) was unusually large. *Third*, of the five relative potency estimates obtained by *post hoc* baseline pain stratification analysis (two from Emich and three from Smith), not one presents a difference between Excedrin and aspirin that is statistically different from 1.00. (RX 211A). Thus, the results of baseline pain stratification analysis appear to confirm that the intensity of pain to be relieved has an important bearing in evaluating the comparative performance of mild analgesics and that one cannot assume that the relative potency estimate derived from a typical bioassay with mixed (slight to

mild to moderate to severe) pain subjects can be reliably used to predict the comparative performance of the two drugs for the relief of mild pain.

In sum, for all the record shows, one could reasonably conclude that Excedrin and aspirin are about eqully effective for the relief of mild pain, including headache.[32]

However, this is not to ignore the well known fact that the practice of medicine is not an exact science but an art, and that clinicians often do form personal judgments on the basis of available data short of adequate scientific demonstration. This is as it should be in the practice of medicine. The application of clinial pharmacology to clinical situations inevitably involves the professional judgment of the clinician and is a matter of trial and error based on long experience, insight and wisdom. Obviously, there may be respectable clinicians who are willing to try Excedrin or Bufferin instead of aspirin on their patients on the strength of the evidence contained in the record. However, that fact adds little to the resolution of the issues in this proceeding.

H. Bufferin's Faster Action Claim Has Not Been Established

Complaint counsel have carried their burden of showing that the faster action claim for Bufferin has not been scientifically established. In support of its faster action claim for Bufferin, Bristol-Myers essentially relies on blood level studies which show earlier and higher serum salicylate concentrations for Bufferin compared to aspirin. Although there is conflicting evidence regarding the blood level data, the main thrust of complaint counsel's argument is that the proposition that an earlier serum concentration level means faster onset or greater intensity of analgesia has not been scientifically established. Although it has been shown for some drugs that a direct correlation exists between blood levels and biologic effect, the existence and the nature of such correlation for aspirin is not

32 It should also be pointed out that these observations regarding pain types and intensity levels apply equally to the pain studies excluded from the record by the administrative judge.

known because of aspirin's unique and complex pharmacokinetic characteristics (Tr. 5942-46, 5957; CX 514 at 35373-74). As plausible as it may sound, such correlation for aspirin remains to be demonstrated.[33] The precise nature and degree of such correlation, if any, with respect to aspirin and its metabolites is particularly important in this case where the issue is whether Bufferin acts faster than aspirin or acts twice as fast as aspirin. These are specific comparative claims and demand specific, direct demonstrations.

Bristol-Myers' reliance on the FDA's bioavailability regulations is clearly misplaced. The issue there simply is whether the FDA should require, after the efficacy and safety of a drug compound is established by well-controlled clinical studies, new or additional clinical studies with respect to every subsequent batch produced by the original maunfacturer or with respect to a chemically identical compound manufactured by another firm. The FDA took the approach that, in these circumstances, a showing of bioequivalence is enough, only because the efficacy of the compound has already been demonstrated by well-controlled human trials. This common sense approach of the FDA cannot be turned into "the FDA says blood level studies are acceptable proof of efficacy," and much less into the FDA says earlier and higher blood levels prove faster and stronger effect." In explaining the

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33 Dr. Beacher described the problem thus:

> Now it's quite clear that we have a product which is incompletely absorbed or extraordinarily absorbed compared to a product which is rapidly absorbed, the former may not ever demonstrate any activity at all. However, as the performance — absorption performance of the two products approaches each other, it becomes increasingly debatable as to the importance of the difference in absorption to the actual therapeutic differences seen. *In the case of analgesics, since we don't know the function which connects analgesic activity with blood level — and in the particular case of aspirin, since we don't even know whether it's the unhydrolized aspirin in the blood or the salicylate in the blood or some peculiar combination of both which is responsible for analgesic activity, it is impossible in the current state of the art to say what the significance of such a difference would be in blood levels in terms of speed of onset of analgesic activity.* (Beacher, Tr. 5942-43). (Emphasis added)

bioequivalence regulations, the FDA Commissioner explicitly disclaimed such inferences.[34]

I. Bufferin's Gentler To a Person's Stomach Claim Has Not Been Established

In support of its comparative safety claims that Bufferin will not upset a person's stomach and that it will cause stomach upset less freguently than aspirin, Bristol-Myers relies on the blood level studies discussed above. Bristol-Myers' argument that since Bufferin is absorbed into the blood stream somewhat faster than aspirin, it will cause less irritation to the stomach than plain aspirin is well grounded in clinical pharmacology. The clinical studies Bristol-Myers relies on, however, are inconclusive. At best they show that, because Bufferin is absorbed into the blood stream somewhat faster than aspirin, Bufferin can reasonably be expected to cause somewhat less gastric discomfort for the small number of consumers in the sub-population who occasionally experience the subjective symptoms of gastric discomfort following aspirin ingestion. However, this proposition has not been adequately demonstrated through well-controlled clinical studies. The studies employing the so-called historical controls add little in this regard. Also, the advertising claim that Bufferin will not upset a person's stomach (Complaint ¶ 9A(4)) is patently false.

The FDA Analgesic Panel's final report corroborates the views recited above regarding the potential occasional benefits of buffered aspirin for the small group who may experience dyspepsia with plain aspirin. The Panel reports:

> Current evidence indicates that properly formulated preparations, those within the proposed antacid and dissolution standards, can be expected to . . . decrease the incidence of subjective gastric intolerance in some of the small percentage of persons in the general population who regularly experience gastric intolerance with OTC doses of plain aspirin tablets.
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> * * *

34 The FDA Commissioner stated, "The bioequivalence regulations are not an attempt to equate evidence of bioequivalence with evidence of relative therapeutic effectiveness." (Tr. II682).

> . . . [T]he evidence although apparently conflicting seems to indicate that buffered aspirin produces a lower incidence of gastric intolerance in some patients but not in all patients who exhibit gastric intolerance with regular aspirin products. The number of patients who might benefit from buffered aspirin compared to standard [plain] aspirin is probably small. (CX 514 at 35470). Also see CX 415A-B.

Furthermore, since Bufferin commercials do not identify the "pain reliever" in Bufferin being compared with "plain aspirin" as aspirin, an advertising claim that Bufferin does not cause or causes less stomach distress than aspirin is highly likely to mislead consumers into a false sense of safety that Bufferin is a product that can be taken without worrying about gastrointestinal side effects. However, aspirin's gastrointestinal side effects are not to be ignored lightly. They are potentially serious, especially when aspirin or aspirin products such as Bufferin are taken in multiple doses or by persons with certain predisposing conditions.

The FDA Analgesic Panel, after reviewing labeling claims for certain buffered and highly buffered aspirin products, including the statements "Faster to the bloodstream" and "Gentle to the stomach," placed in Category II any statement that suggests or represents a buffered product as having a more rapid absorption or as preventing any side effects to the stomach, and recommended that labeling claims be restricted to the following Category III statements: "Faster to the blood stream than plain aspirin" and "Provides ingredients that may prevent the stomach distress that plain aspirin occasionally causes but should not be taken by certain individuals with stomach disorders as cautioned elsewhere on the label." (CX 514 at 35480) Also see CX 514 at 35470, 35474.

J. Tension Relief Claims For Bufferin, Excedrin and Excedrin P.M. Do Not Have A Reasonable Basis

The main thrust of Bristol-Myers' argument with respect to the tension relief claims is that its advertisements for Bufferin, Excedrin and Excedrin P.M. did not make those claims. Nev-

ertheless, Bristol-Myers attempted to show that the tension relief claim for Bufferin, Excedrin and Excedrin P.M. had a reasonable basis when made. In my view, the evidence Bristol-Myers relies on is either obsolete or unreliable. The modern view for some years has been that aspirin and/or the other ingredients in Excedrin, or Excedrin P.M., either singly or in combination, are not recognized tension recognized relievers.

The record as a whole clearly shows that Bufferin, Excedrin or Excedrin P.M. will not relieve tension. Dr. Rickels, an eminent authority in the study of psychopharmacologic drugs, testified that aspirin or Excedrin will not relieve tension or emotional anxiety. In a well-controlled, double-blinded clinical trial evaluating the effects of aspirin on tension, aspirin was found not to be significantly superior to placebo in the relief of moderate tension (Rickels, Tr. 6500-17). The medical literature confirms that aspirin cannot be expected to relieve tension. The FDA OTC Internal Analgesics Panel concluded that aspirin was "clearly ineffective" for "nervous tension" (CX 514 at 35355). Also, the FDA OCT Sedative Panel determined that aspirin was "ineffective" as a "day-time sedative" product, which was defined as one claiming "mood-modifying indications such as for the relief of occasional simple nervous tension'." (CX 513E, Z002; Tr. 6538). The Sedative Panel reached the same conclusion with respect to acetominophen and salicylamide (CX 513E; Tr. 6540). The NAS/NRC Drug Efficacy Study Group reviewed medical-scientific evidence regarding Bufferin and reached a negative conclusion with respect to Bufferin's tension relieving effect (CX 511F). The medical literature Bristol-Myers relies on is woefully dated and does not constitute a reasonable basis for Bristol-Myers' tension relief claim that continued from the early 1960's through 1970.

With respect to Excedrin P.M., the only difference between it and Excedrin is that it contains Methapyrilene Fumarate instead of caffeine. The three ingredients Excedrin P.M. has in common with Excedrin (aspirin, acetaminophen and salicylamide) are not effective tension relievers.

Methapyrilene is not an effective tension reliever (daytime sedative). Although there is some evidence indicating that methapyrilene may be an effective mild sedative in animals, the FDA Sedative Panel was divided on the issue of methapyrilene's efficacy and safety as a mild OTC daytime sedative in humans. A minority of the Panel considered it to be ineffective, but the majority placed it in Category III, allowing manufacturers further opportunity to develop favorable clinical studies. However, it was the unaminous opinion of the Panel that the studies would not show methapyrilene's efficacy for the relief of nervous tension. Dr. Rickels, the Panel's chairman, testified that, since no further research on this issue has been forthcoming, all members of the panel now believe that methapyrilene should be placed in Category II as a daytime sedative (Tr. 6541-51).[35]

K. Unfairness And The Substantial Question Theory

Complaint counsel argue that a comparative claim of efficacy or safety of an OTC analgesic product, made expressly or by implication, constitutes a representation that the claim is scientifically established. They further argue that, with respect to the various comparative claims for Bufferin, Excedrin and Excedrin P.M., the claims are not established because there exists a substantial medical-scientific question about their validity among scientists who by their training and experience are competent to judge the validity of such claims. Complaint counsel finally argue that the existence of a substantial question is a material fact and that an advertisement which carries such a comparative claim without disclosing the existence of a substantial question is not only false within the meaning of Sections 12 and 5 of the FTC Act but also an unfair act or practice within the meaning of Section 5.

I am persuaded that the substantial question theory outlined hereinabove is, in the particular factual context of this case, a

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35 Apparently Bristol-Myers is in the process of reformulating Excedrin P.M. without methapyrelene since the FDA determined earlier this year that methapyrelene is a carcinogen in animals. See *The Wall Street Journal*, June 7, 1979, p. 23, c.2-4; June 11, 1979, p. 13, c.1.

reasonable application of the "reasonable basis" doctrine, which has been judicially sanctioned. *Pfizer, Inc.*, 81 F.T.C. 23 (1972); *Firestone Tire & Rubber Co.*, 81 F.T.C. 398 (1972), *aff'd*, 481 F.2d 246 (6th Cir. 1973), *cert. denied*, 414 U.S. 1112 (1973); *National Dynamics Corp.*, 82 F.T.C. 488 (1973), *aff'd*, 492 F.2d 1333 (2d Cir. 1974), *cert. denied*, 419 U.S. 993 (1974).

The basic rationale of *Pfizer* is that an affirmative product claim carries with it an implied representation that the advertiser possessed and relied on a reasonable basis for the claim when the claim was made and that such an advertising claim in the absence of a reasonable basis is an unfair act or practice in violation of Section 5 within the meaning of Section 5. See *FTC* v. *Sperry & Hutchinson Co.*, 405 U.S. 233, 234 (1972). The reasonabls basis requirement applies even if an advertisement claim is in fact true. 81 F.T.C. at 63. Also see *id.* at 67-68.

In *Pfizer*, a case involving a simple efficacy claim for a topical OTC anesthesic preparation, the Commission reasoned that (81 F.T.C. at 62):

> "Given the imbalance of knowledge and resources between a business enterprise and each of its customers, economically it is more rational, and imposes far less cost on society, to require a manufacturer to confirm his affirmative product claims rather than impose a burden upon each individual consumer to test, investigate, or experiment for himself. The manufacturer has the ability, the knowhow, the equipment, the time and resources to undertake such information by testing or otherwise—the consumer usually does not.
>
> "***Absent a reasonable basis for a vendor's affirmative product claims, a consumer's ability to make an economically rational product choice, and a competitor's ability to compete on the basis of price, quality, service or convenience, are materially impaired."

The Commission, therefore, concluded that as a matter of marketplace fairness, a consumer is entitled to rely upon the manufacturer to have a reasonable basis for making performance claims. *Id.*

In determining what constitutes "a reasonable basis," the Commission set forth a number of guidelines in *Pfizer*. First, the Commission made it clear that the requirement is not solely a "reasonable man" test. The reasonable basis requirement questions both the reasonableness of an advertiser's actions and the adequacy of evidence upon which such action is based.[36] The reasonable basis standard is essentially a fact issue to be determined on a case-by-case basis, and depends on such overlapping considerations as: (1) the type and specificity of the claim made (*e.g.*, safety, efficacy, dietary, health, medical); (2) the type of product (*e.g.*, food, drug, potentially hazardous products); (3) the possible consequences of a false claim (*e.g.*, personal injury); (4) the degree of reliance on the claim by consumers; and (5) the type and accessibility of evidence adequate to form a reasonable basis for the particular claim.[37] For some types of claims and for some types of products, the only reasonable basis "in fairness and in the expectation of the consumer" would be an adequate and well-controlled scientific test.[38]

This proceeding involves comparative and superlative efficacy and safety claims for aspirin-based OTC internal analgesic products. Such drugs as a class is known to be the most popular OTC drug in this country. American consumers purchase some 19 billion dosage units annually. Although they are generally safe and effective for the relief of minor pain and headache pain and for the reduction of inflammation and fever, they are potent drugs and have numerous adverse side effects, some of which are serious and can be life-threatening.

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36 See *id.* at 64.

37 *Id.* at 64.

38 *Id.* at 64, 66-67.

Bufferin and Excedrin are among the major and heavily advertised aspirin-based OTC internal analgesic products in this country. Against this background, what is the reasonable level of substantiation required for a claim that Bufferin is faster acting than aspirin and causes less gastric distress than aspirin and that Exedrin and Excedrin P.M. are stronger than aspirin?

Consumers obviously have no means of verifying the truth of such a pharmacological-clinical superiority claim for themselves. Moreover, consumers are willing to pay, and do pay, a significantly higher price for the alleged superiority of these products. If the alleged superiority is not established, the consumer's evidently widespread self-medication with the allegedly faster/ safer, extra-strength OTC analgesic products is not only pharmacologically superfluous and economically wasteful but also is accompanied by significant health hazards (increased potential for adverse side effects).

In my view, in the circumstances of this case, such a comparative claim constitutes, "in fairness and in the expectation of the consumers" and as a matter of law, an implied representation that the manufacturer has a sufficient kind and degree of substantiation for its claim. To state it another way, the consumers of OTC analgesic products are entitled, as a matter of marketplace fairness, to rely upon the manufacturer to have a sufficient kind and level of substantiation for the claim. In the circumstances of this case, the only sufficient substantiation for the claim is that the claim is accepted as established by the medical-scientific community on the basis of well-controlled clinical studies.

Furthermore, with respect to Bufferin, a number of advertisements expressly claimed that the alleged superiority of Bufferin has been established." *E.g.*, CX 99. Also, a number of Bufferin and Excedrin advertisements referred to clinical or hospital tests, and used chemical formulas, graphs, and anatomical models as a support for superiority claims for Bufferin and Excedrin. Therefore, it is reasonable to infer that these advertisements conveyed to the consumer a distinct message that

the superior features of Bufferin or Excedrin being discussed in these advertisements have been sufficiently proven by medical-scientific evidence.[39]

The record is clear that, with respect to OTC internal analgesic products, the medical-scientific community requires two or more well-controlled clinical studies using appropriate pain models, one of which is a headache pain model.

It is also clear that the absence of that kind and level of substantiation leaves a substantial question regarding a claim of comparative efficacy or safety, and that the existence of such a question is a material fact, of which the failure to disclose will render an advertisement deceptive. A substantial question is a fact issue to be determined on a case-by-case basis. In this case, complaint counsel argue essentially that a substantial question exists because the comparative or superlative efficacy or safety claim is not accepted as true or as a proven scientific fact by the vast majority of medical scientists who are by their training and experience competent to judge the scientific validity of such claims. In this sense, a substantial question does not mean unanimity of medical-scientific opinions. Nor do occasional dissents make out a substantial question. It relates rather to the quality and quantum of medical-scientific evidence in support of a proposition. In the field of clinical pharmacology, it is generally agreed that two or more well-controlled clinical demonstrations showing statistically significant results are suffiient to establish a medical-scientific proposition. The record as a whole shows that in the absence of that level of supporting data, the medical scientists are unwilling to accept a proposition as true or proven.

Furthermore, the rationale of the substantial question theory as applied to advertising claims for comparative efficacy or

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39 There is testimony in the record which suggests that consumers generally believe that advertising claims for drug products are supported by adequate medical-scientific substaniation and that otherwise the advertisers would not be permitted to make such claims by the regulatory authorities. (Tr. Ross) Also see *Standard Oil of California*, 84 F.T.C. 1401, 1473 (1974); *Simeon Management Corp.*, 87 F.T.C. 1184, 1230 (1976), *aff'd*, *Simeon Management Corp.* v. *FTC*, 579 F.2d 1137, 1145-46 (9th Cir. 1978).

safety of OTC analgesic products is not only consistent with congressional policy of drug regulation embodied in the 1962 Amendment to the Food, Drug and Cosmetic Act and implemented by the FDA, but also is consonant with the findings and recommendations of the FDA OTC Internal Analgesics Panel.

In Section 505(d) of the Food, Drug and Cosmetic Act, as amended (21 U.S.C. § 355), Congress mandated a "substantial evidence" standard for granting a new drug application (NDA) with respect to all drugs, including new OTC drugs. Congress defined "substantial evidence" of drug efficacy in Section 505(d) as

> "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have . . . ."

Under the HEW regulations promulgated to implement that congressional policy, the FDA has set forth several principles which, in its words,

> "have been developed over a period of years and are recognized by the scientific community as essentials of adequate and well-controlled clinical investigations. They provide the basis for the determination whether there is 'substantial evidence' to support the claims of effectiveness for 'new drugs' . . . ." 21 CFR § 314.111(a)(5)(ii).

It should be pointed out that many of the FDA's "principles" closely parallel the very criteria testified to by the expert witnesses in this proceeding as important elements of a well-controlled clinical study. Cf. 21 CFR § 314.lll(a)(5)(ii)(a) through (c) and F. 366-94. Furthermore, these FDA requirements have been consistently upheld by courts. See *e.g.*, *Weinberger* v. *Bentex Pharmaceutical, Inc.*, 412 U.S. 645 (1973); *Ciba Corp.* v. *Weinberger*, 412 U.S. 640 (1973); *Weinberger* v. *Hynson, Westcott and Dunning, Inc.*, 412 U.S. 609 (1973); *United States* v. *Articles of Food and Drug Con-*

sisting of Coli-Trol-80, etc., 518 F.2d 743 (5th Cir. 1975); *Sterling Drug, Inc.* v. *Weinberger*, 503 F.2d 675 (2d Cir. 1974).

These well-established criteria for establishing the effectiveness of new prescription and non-prescription drugs have been recently reaffirmed by the FDA when it promulgated review procedures for OTC drugs by various panels of experts, including the Panel on Analgesic, Antipyrstic and Antirheumatic Products, and when the FDA initiated rulemaking proceedings known as "monograph" proceedings. See 21 CFR § 330.10(a)(4)(ii). Pursuant to this mandate, the FDA OTC Internal Analgesics Panel set forth specific criteria for well-controlled clinical studies required to establish the efficacy and safety of active agents used in OTC analgesic products. The Panel's criteria closely resemble the criteria extensively testified to by various experts at trial in this proceeding. More specifically, "to establish Category I status for a Category III compound," the Panel required "at least two studies by independent investigators" which are conformed to a number of specific criteria. These criteria are virtually identical to the ones testified to by expert witnesses in this proceeding. *Cf.* CX 514 at 35444-45 and F. 366.

Thus, the FDA, pursuant to congressional policy embodied in the Food, Drug and Cosmetic Act, requires at least two well-controlled clinical demonstrations of efficacy for both new prescription drugs and new OTC drugs. The FDA has reaffirmed the same standard in connection with its OTC drug review with respect to the issue of *simple* efficacy. The FDA OTC Internal Analgesic Panel recommends the same standard for OTC analgesic products for labeling with respect to the issue of *simple* efficacy and safety. It is eminently reasonable for the Commission to apply the same standard to advertising claims of *comparative* efficacy or safety for OTC analgesic products involved in this proceeding. It would be unreasonable for the Commission to accept for drug advertising a standard which is less than what the FDA requires for labeling.

The "substantial question" standard of unfairness in the context of this proceeding focuses upon the fairness of com-

parative superiority claims for OTC aspirin products which are therapeutically insignificant modifications of well known aspirin, all having the same general actions or virtually the same efficacy and safety factors when the claimed superiority is not scientifically established but capitalized upon in order to achieve some marketing advantage, by advertisers who know that consumers are not in a position to evaluate the claim and must trust that the superiority claim is scientifically established.

Since the record shows that the standards of clinical testing of analgesics have been well established since the early 1960's, the unfairness of the challenged comparative claims should be determined primarily on the basis of whether the claimed comparative proposition met these standards. Therefore, the fact that the claim is based on sound pharmacological reasoning, or has some support among experts or in medical literature is not enough to meet those specific standards relating to well-controlled clinical demonstration of superior efficacy or safety.

Finally, the presence of aspirin in these products is a material fact from an economic point of view. The record shows that a substantial number of consumers do not know that the analgesic ingredient in Bufferin and Excedrin is aspirin. Obviously, if this fact were known to consumers, that fact would be an important factor in making a choice between higher priced aspirin products and lower priced aspirin. In this sense as well, the presence of aspirin in these products is a material fact which ought to be disclosed in future advertisements. Also see section M, *infra*.

L. The Establishment Claims Related to Bufferin, Excedrin and Excedrin P.M. Will Be Deceptive Unless Qualified By An Affirmative Disclosure Of the Existence Of A Substantial Question

It is axiomatic that the Commission's power under Sections 5 and 12 to proscribe deceptive or misleading advertisements includes the power to require affirmative disclosure of a mate-

rial fact in future advertisements of a product claim. In any sense, a fact is material if non-disclosure of that fact makes a claim patently deceptive and misleading. *E.g.*, *ITT Continental Baking Co.* 83 F.T.C. 865, 965 (1973), *rev'd in part* 532 F.2d 207 (2d Cir. 1976); *FTC v. Royal Milling Co.* 288 U.S. 212, 216-17 (1933); *Pep Boys-Manny Moe & Jack Co. v. FTC* 22 F.2d 158, 161 (3d Cir. 1941). *Cf.*, *National Commission On Egg Nutrition*, 88 F.T.C. 89, 192-94 (1976), *modified*, 570 F.2d 157 (7th Cir. 1977). In this case, an establishment claim, express or implied, would clearly be misleading and deceptive unless qualified by disclosure of the fact that a substantial question exists regarding its scientific validity. The fact that the superiority claims have not been scientifically established or that there is a substantial question among scientists who by training and experience are qualified to evaluate such claims, is a material fact which must be disclosed to consumers. The fact that there is a substantial scientific question about the claim obviously is a vitally important factor for consumers in deciding which OTC aspirin products to buy. The existence of a substantial question is even more material, indeed crucial in this case because consumers cannot be expected to evaluate the validity of these establishment claims.

Under the provisions of Section 15 of the FTC Act, the failure to disclose facts which are material in light of representations made in drug advertising constitutes a false advertisement in violation of Section 12. The existence of a substantial question regarding the challenged claims of comparative efficacy and safety is a material fact in light of the establishment representations made in the advertisements for Bufferin, Excedrin and Excedrin P.M. The failure to disclose the existence of that substantial question has the tendency and capacity to mislead consumers to believe that the challenged comparative claims can be accepted without qualification. Therefore, the unqualified superiority claims were misleading and in violation of Sections 5 and 12 of the Federal Trade Commission Act.

M. The Presence of Aspirin In Bufferin, Excedrin and Excedrin P.M. Is A Material Fact Which Should Be Disclosed In Advertisements For These Products

In the language of Section 15 of the FTC Act facts may be "material" in light of the "consequences which may result from the use of the commodity to which the advertisement relates" under "customary or usual conditions" 15 U.S.C. § 55(a)(i). The presence of aspirin in Bufferin, Excedrin and Excedrin P.M. is a material fact in that sense and, therefore, the failure to disclose that fact is a violation of Section 12 of the FTC Act. There is a sharp dispute among the parties as to both the incidence and severity of adverse side effects and the utility of an advertising disclosure requirement, especially in view of the fact that the labels for these products list aspirin as an ingredient, in accordance with FDA labeling regulations.

Aspirin is said to be the most popular OTC drug in this country. It is estimated that almost 19 billion dosage units are sold annually. Without a doubt, aspirin is a highly effective and relatively safe analgesic agent. Its versatility and usefulness in terms of a risk-benefit ratio have been demonstrated over many decades. However, aspirin is also a potent drug and has a number of serious adverse side effects. Several expert witnesses in this case discussed the nature and extent of the principal side effects (F. 645-671). The FDA OTC Internal Analgesics Panel's report contains a handy compendium of aspirin side effects in eight major areas of concern (CX 514 at 35383-35411). They include: effects on various organ systems such as the gastrointestinal tract central nervous system, kidney, liver and the blood; specialized effects on hypersensitive persons, persons with certain disease states or during pregnancy; and effects when used with other drugs. Some of these side effects are known to be serious and even life-threatening to many high risk subjects. The record shows that aspirin-induced or related hospital emergencies have reached alarming proportions. For example, in a recent survey, aspirin was found to be the second most frequent drug involved in adverse

effects of drugs that were serious enough to require hospitalization. Two out of every 1000 hospital admissions were attributed to aspirin (CX 514 at 35392).

Consonant with its concern about the varied and substantial adverse effects of aspirin, the FDA OTC Internal Analgesics Panel recommended that appropriate warnings and cautionary statements be included on labels of all aspirin-containing OTC products (CX 514 at 35393-94). A number of these warnings and cautionary statements say that aspirin-containing products should not be taken under certain conditions or by certain persons without a prior consultation with a physician. For the consumer to whom the warnings and cautions are intended, his knowledge that a given product contains aspirin is crucial. However, the record clearly shows that a large number of consumers are unaware of the fact that many OTC analgesic products, including Bufferin and Excedrin contain aspirin and that a large number of consumers neglect to read labels of such products. These facts, involving important questions of public health, make aspirin ingredient disclosure imperative in all advertisements for aspirin-containing OTC products. In my view, the frequency and severity of two types of adverse effects which can be life-threatening, make such advertising disclosure mandatory. They are aspirin-induced massive gastrointestinal bleeding and acute asthmatic attacks in aspirin-intolerant persons.[40]

Aspirin-Related Massive Gastrointestinal Bleeding

Although the mechanism of action of aspirin upon the gastrointestinal tract resulting in sudden, massive bleeding is not definitively understood, it is generally agreed that orally administered aspirin, as well as intravenously administered aspirin, can cause sudden, massive and life-threatening bleeding in the gastrointestinal tract, especially in persons with certain predisposed conditions such as dyspepsia, gastrointestinal le-

40 The record shows that a relatively small amount of aspirin (3 mg.) can cause a severe reaction, including anaphylactic shock, in aspirin-intolerant persons (F. 662).

sions, peptic ulcers or other bleeding problems in the gastrointestinal tract (F. 652).

A recent survey showed aspirin to be the second most frequent drug involved in all hospitalizations due to the adverse effects of drugs. Two out of every 1000 such hospital admissions were attributed to aspirin. Massive gastrointestinal bleeding was second only to digitalis intoxication as the most frequent cause of drug-related hospitalization and aspirin and aspirin-containing products were involved in 60% of the cases. Moreover the mortality rate associated with this condition is high. Death occurs in 4 to 10% of all patients with massive gastrointestinal bleeding, including those associated with aspirin ingestion. Even higher mortality rates are shown in those patients who require surgical intervention to stop the massive internal bleeding (CX 514 at 35392). Furthermore, there is evidence that aspirin can cause gastric ulcers when taken in large doses and aspirin may cause a specific kind of ulcer not seen in its absence. Gastric ulcer is a serious disease with significant morbidity, and often requires surgery on the stomach. By conservative estimate, aspirin ingestion results in 10 out of every 100,000 users developing a gastric ulcer, requiring hospitalization. Levy's Boston Collaborative group study also estimated that one-eighth of all gastric ulcers were aspirin-related (CX 514 at 35390). Although these incidences are relatively small in terms of absolute numbers, they clearly present a serious public health problem. Therefore, the FDA OTC Internal Analgesics Panel recommended that all products containing aspirin should bear a warning: "*Caution*: Do not take this product if you have stomach distress, ulcers or bleeding problems except under the advice and supervision of a physician." (CX 514 at 35395).The aspirin-related gastrointestinal massive bleeding is compounded by aspirin's recently known anticoagulation effect (CX 514 at 35385).

Aspirin-Intolerant Individuals

Aspirin hypersensitivity reactions (or aspirin-intolerant reactions) are varied. They include: effects on the respiratory tract ranging from shortness of breath to severe asthmatic at-

tacks; effects on the skin such as urticaria, agnioedema, edema and rash: and anaphylactic shock involving laryngeal swelling, blockage of air pathways and a sudden drop in blood pressure which can result in death if not treated rapidly (F. 661). Buffering will not mitigate aspirin's asthmatic side effects (F. 663). Although the incidence of aspirin intolerance in the general population is relatively small, it clearly presents a serious and substantial problem of public health.Therefore the FDA OTC Internal Analgesics Panel recommended that labels for all products containing aspirin include the warning: "This product contains aspirin. Do not take this product if you are allergic to aspirin or if you have asthma except under the advice and supervision of a physician." (CX 514 at 35399).

In addition in 1973 the American Academy of Allergy, a professional body composed of some 2,200 allergy specialists in the United States, adopted a resolution recommending that a "formulation containing aspirin and advertisements promoting the formulation should clearly indicate that the preparation contains aspirin and that aspirin can be harmful to some persons." (CX 514 at 35398; Tr. 2608-13). The FDA OTC Internal Analgesics Panel expressed its agreement with this resolution (CX 514 at 35398-99).[41] The 1973 resolution of the American College of Allergists, another professional body composed of allergy specialists, is also in accord with the 1973 resolution of the American Academy of Allergists (Farr Tr. 2613, 3650).

Against the unanimous judgment of two responsible professional organizations of specialists and the FDA OTC Internal Analgesics Panel, Bristol-Myers argues that such advertising disclosure is totally unnecessary because (1) the incidence of aspirin intolerance or massive gastrointestinal bleeding is small and (2) to the extent some consumers are susceptible to such side effects, they can be counted on to read OTC drug labels. These arguments are unacceptable.

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41 The Panel also "strongly urges the Federal Trade Commission to require that cautionary language and warnings developed by the Panel be given emphasis in commercial advertising more so than is currently being done. . . ." (CX 514 at 35356).

First, with respect to aspirin-intolerance, the incidence figures for asthmatics in the record varies from a low of 0.1% to a high of 28%.[42] Even if we were to take the low range, it represents close to one-quarter of a million persons who will suffer a severe adverse reaction from aspirin ingestion, which can be life-threatening. When we take into account the significant number of people who may suffer serious gastrointestinal side effects the considerations for mandating advertising disclosure of aspirin content is overwhelming.

Respondents' argument that consumers know that Bufferin, Excedrin and Excedrin P.M. contain aspirin is unpersuasive. There is evidence that a substantial portion of consumers do not know that OTC analgesic products, such as Bufferin and Excedrin, contain aspirin. This is not surprising in view of the long history of Bufferin and Excedrin advertisements which carefully avoided any hint that it contains aspirin and suggested by implication that their analgesic ingredient is something special and that it is something other than aspirin. Similarly unpersuasive is respondents' argument that those consumers who should not take aspirin are advised not to take aspirin and instructed to read labels by their physicians. First many aspirin-intolerant persons are not aware of their condition in this respect until they experience a severe adverse reaction. Second, the number of consumers who do not read labels before they take an OTC product is as large as, if not larger than, those who read the labels. Similarly, "read-the-label" campaign does not tell consumers that these products contain aspirin. It simply exhorts consumers to read all OTC drug labels. What is needed is a direct and clear statement in all Bufferin/Excedrin/Excedrin P.M. advertising that they contain aspirin.

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42 Tr. 1495. Dr. Stevenson testified that 10% is a conservative figure. The record as a whole supports the conclusion that 10% is probably the best estimate. On this basis, the number of persons who are aspirin-intolerant reaches some 2.25 million.

N. Caffeine Disclosure Statements In Excedrin Advertisements Are Not Required

Caffeine has been used widely as a combination ingredient in analgesic products, including Excedrin. When used as an adjuvant, caffeine is safe at a single dose of 65 mg. not to exceed 600 mg. in 24 hours, although its efficacy as an analgesic has not been sufficiently demonstrated.[43] Although chronic caffeine toxicity has not been observed in humans, some resistance to caffeine is known to develop. Tolerance to caffeine is likely to develop with daily use. Caffeine, long known as a central nervous system stimulant, is also a cardiac stimulant. It is known to cause increased gastric secretion in the stomach and possibly contribute to gastric bleeding. It has been suggested that caffeine can cause peptic ulcers and should be avoided by patients with peptic ulcers. Caffeine also inhibits platelet aggregation and its use in patients with gastric bleeding is not recommended.[44] Caffeine is associated with an increase in blood pressure.

However, the record as a whole does not show that the incidence and severity of adverse effects of caffeine are of such magnitude as to make the existence of caffeine in Excedrin a material fact which should be dislosed in Excedrin advertisements. Furthermore an affirmative dislosure requirement is a form of prior restraint upon commercial speech and should not be lightly imposed in the absence of a clear showing that nondisclosure will make the advertisement deceptive or unfair to the consumer or raise a substantial health or safety problem.

O. Bristol-Myers' Legislative Preclusion Argument Is Without Merit

Bristol-Myers argues that the legislative history of Sections 12 and 15 of the FTC Act precludes the Federal Trade Commission from imposing upon Bristol-Myers any liability for

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43 CX 514 at 35482-83.

44 CX 514 at 35484-85.

failing to disclose the existence of a substantial question regarding its comparative claims in advertisements containing such claims for Bufferin, Exedrin and Excedrin P.M. (BMM, III, 3-7) At first blush, Bristol-Myers' argument appears plausible. However, a closer examination of the pertinent legislative history leaves no doubt that what Congress had in mind in 1938 was to specify a statutory defense, not to create an exemption, in the amended Act. When Congress was considering the legislation that became Section 15 of the amended Federal Trade Commission Act, it contemplated including a statutory defense in cases where there was a division in the medical community as to the truth of a product claim if the advertiser disclosed the existence of the conflicting opinion in his advertisement. However, Congress was persuaded that this was not necessary because in all cases the government will have to carry the burden of showing that, absent such disclosure, the advertisement as a whole is misleading or deceptive. (BMM, III, 4-5) It was understood that nothing in the paragraph of the House version was to be construed as "requiring" the making of such disclosure statement as to the difference of opinions. However, nothing in the legislative history can be reasonably construed to support the proposition that a finding of liability under Sections 12 and 15 is precluded where an advertisement is in fact misleading and deceptive unless the existence of such a question is disclosed in the advertisement. Any other reading of the legislative history would virtually vitiate the central purpose of the 1938 amendment and result in imputing a legislative exemption where none was intended by Congress. The language of the House Report on the Wheeler-Lee Amendment clearly demonstrates a congressional intention to confer upon the FTC a broad mandate to regulate misleading advertising regarding foods and drugs:

> The provisions of this bill covering false advertising are far reaching but we believe entirely warranted, necessary for the effective control of illegitimate advertising and yet drawn with due regard to the rights of legitimate advertising.
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> * * * * *

> The advertisement amendments to this bill revolve around the definitions of a "false advertisement" in Section 15. A false advertisement is defined as one "which is misleading in material respect." Certain specified matters are to be considered in determining whether or not an advertisement is misleading. This definition is very broad. It will be noted that a fraudulent intent is not a necessary element of a false advertisement. The essential elements of a false advertisement are that it is misleading and *misleading in a material respect*. It places on the advertiser the burden of seeing that this advertisement is not misleading.
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> * * * * *
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> The definition is broad enough to cover every form of advertisement deception over which it would be humanly practicable to exercise governmental control. It covers every case of imposition on a purchaser for which there could be a practical remedy. It reaches every case from that of inadvertent or uniformed advertising to that of the most subtle as well as the most vicious types of advertisements.[45]

Respondent's implied exemption argument is also refuted by the fact that where Congress intended to create an exemption from the operation of the statute, it did so explicitly.[46]

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45 H.R. Rep. No. 1613, 75th Cong., 1st Sess. (1937) 4-5.

46 See, *e.g.*, 15 U.S.C. 55(a)(1) (1970):

> The term "false advertisement" means an advertisement, other than labeling. . . . No advertisement of a drug shall be deemed false if it is disseminated only to members of the medical profession, contains no false representation of a material fact, and includes, or is accompanied in each instance by truthful disclosure of the formula showing quantitatively each ingredient of such drug.

See also 21 U.S.C. § 502(n)(3)(B) (1970):

> No advertisement of a prescription drug . . . shall with respect to the matters specified in this paragraph or covered by such regulations, be subject to the provisions of Sections 12 [-] 17 of the [FTC] Act. . . .

Furthermore the Commission's authority under Section 12 of the Act to require an advertiser to disclose the existence of a medical controversy in appropriate cases has been upheld by the Seventh Circuit in 1977. *See National Commission on Egg Nutrition*, 88 F.T.C. 89, 193-194 (1976), *mod. in part*, 570 F.2d 157, 164-65 (7th Cir. 1977), *cert. denied*, U.S. (1978).

We need not dwell on Bristol-Myers' argument that under Section 15(a) of the amended FTC Act, the Commission has no power to require disclosure of any drug ingredient in advertising because the FDA was given an exclusive jurisdiction over labeling of drug products. The issue in this case is not what the contents of any label for Bristol-Myers' OTC analgesic products should be, but whether the existence of aspirin in these products is a material fact which in light of other representations contained in the ads should be disclosed. Simply put, the issue in this case is false or misleading advertising, not misbranding.

P. Bristol-Myers' Constitutional Objections To The Substantial Question Disclosure Requirements Are Without Merit

Bristol-Myers' free speech argument in opposition to the requirement that comparative claims for Bufferin, Excedrin and Excedrin P.M. be accompanied by appropriate disclosures regarding the existence of a substantial question, is not well founded. It is now well established that commercial speech is entitled to the full protection of the First Amendment. *Virginia State Board of Pharmacy v. Virginia Citizens Consumer Counsel*, 425 U.S. 748 (1976). However, it is also well established that commercial speech that is false or misleading forfeits that protection. *Id.* at 771 n. 24; *Warner-Lambert Co. v. F.T.C.*, 562 F.2d 749 (D.C. Cir. 1977), *reversing in part*, *Warner-Lambert Co.*, 86 F.T.C. 1398 (1975), *cert. denied*, 46 U.S.L.W. 3616 (April 14, 1978); *National Commission on Egg Nutrition*, 88 F.T.C. 89, 195-99 (1976), *modified* 570 F.2d 137 (7th Cir.1977), *cert. denied*, U.S. (1978).

In the cases involving commercial speech, the First Amendment test is whether the proposed prior restraint will prohibit truthful speech or otherwise unduly tend to inhibit truthful speech. In this proceeding, it was found that respondents' comparative claims of superior efficacy and safety have not been established and that the existence of a substantial question with respect to these advertising claims is a material fact, of which the failure to disclose would render the advertising claim deceptive and misleading. In these circumstances, the requirement for affirmative disclosure of that material fact is well within the long established proscription against deceptive commercial speech. Bristol-Myers' argument that such a requirement in the context of the substantial question theory would have the effect of chilling truthful speech is therefore without merit.

None of the recent commercial speech cases cited by Bristol-Myers (BMM-VIII) suggests that the Commission under Sections 5, 12 and 15 of the FTC Act may not require an affirmative disclosure to prevent a claim from being misleading or that the Commission must prove a claim to be false before imposing restraints on future dissemination of that claim. In fact, the Court in recent years has reaffirmed the view set forth in *Virginia State Board*, 425 U.S. at 771-72 n. 24.[47] Most recently, in *Friedman v. Rogers*, 47 U.S.L.W. 4151 (Feb. 20, 1979) the Court stated:

> . . . Equally permissible are restrictions on false, deceptive, and misleading commercial speech. *Id.* at 4153.
>
> Regarding the permissible extent of commercial speech regulation, the Court observed in *Virginia Pharmacy* that certain features of commercial speech differen-

47 In *Young v. American Mini Theatres*, 427 U.S. 50 (1976):

> [R]egulatory commissions may prohibit businessmen from making statements which though literally true, are potentially deceptive. *Id.* at 68-69 n. 31.

And again in *Bates v. State Bar of Arizona*, 433 U.S. 350 (1977):

> We do not foreclose the possibility that some limited supplementation, by way of warning or disclaimer or the like, might be required . . . so as to assure that the consumer is not mislead. *Id.* at 380.

> tiate it from other varieties of speech in ways that suggest that "a different degree of protection is necessary to insure that the flow of truthful and legitimate commercial information is unimpaired." [citation]
>
> * * *
>
> Commercial speech, because of its importance to business profits, and because it is carefully calculated, is also less likely than other forms of speech to be inhibited by proper regulation. These attributes . . . indicate that it is "appropriate to require that a commercial message appear in such a form . . . as [is] necessary to prevent its being deceptive. . . .They may also make inapplicable the prohibition against prior restraints." [citations omitted] *Id.* at 4154.

Also, the constitutional challenge against the reasonable basis requirement in this case is misdirected for the reason that the tension relief claims related to Bufferin and Excedrin not only lacked a reasonable basis but also were untrue. While the free speech protection extends to commercial speech and truthful speech may not be banned outright under a claim of substantial governmental interest," what is being proscribed here is not "truthful speech" by any stretch of the imagination but affirmative medical-scientific claims for drug products which are based on some favorable clinical studies and at times simply on pharmacological theory. Clearly there is an important distinction between "truthful speech" and a product claim based on medical-scientific theory or on questionable experimental data. Free speech is a keystone of free political institutions and must be guarded with steadfast vigilance. However, it may not be invoked to insulate from proper regulation commercial speech which is misleading and unfair to the consumer.

Q. Product Images of Bufferin, Excedrin And Corrective Advertising

Complaint counsel contend that: (1) a substantial number of consumers have an image of Bufferin as a faster and gentler pain reliever than aspirin and an image of Excedrin as a faster

and more effective pain reliever than aspirin; (2) these images are due in substantial part to Bristol-Myers' misleading advertising claims made over a period of many years; (3) these product images will persist in the absence of corrective advertising designed to convey to consumers a corrective message that these products' superior speed, efficacy or safety is not scientifically established. Respondents vigorously dispute complaint counsel's argument. It is my determination that (1) the record is devoid of any evidence from which it may reasonably be inferred or which tends to show that any consumer is likely to have an "establishment" image about any product involved in this proceeding; (2) although the record shows that a substantial number of consumers had an image of Bufferin and Excedrin as tension relievers, the empirical evidence in the record suggests that Bristol-Myers' advertisements may not have played a substantial role in creating or maintaining that image; and (3) in any event the tension advertisements for Bufferin and Excedrin ceased by 1970 and there is no solid basis for requiring any corrective advertising in this case.

1. Product Images Their Sources And Duration

The mere fact that Bristol-Myers made the challenged advertising claims for a long period of time supports a fair inference that consumers will have an image of Bufferin as a faster and gentler pain reliever than aspirin and an image of Excedrin as faster and more effective pain reliever than aspirin.[48] This inference is further confirmed by some empirical data in the record.

The record as a whole clearly supports the conclusion that consumers have had these product images about Bufferin and Excedrin for some years. The five commercial market research studies (CXS 310, 346, 1058 and 1059) conducted between 1967 and 1970 by various reputable firms for different marketers of aspirin products (including Bristol-Myers) to-

48 *Cf. Warner-Lambert Co.*, 86 F.T.C. 1398, 1501-02, 1503 (1975), *rev'd in part*, 562 F.2d 749, 762 (D.C. Cir. 1977), *cert. denied*, 46 U.S.L.W. 3616 (U.S. April 14, 1978); *National Commission on Egg Nutrition v. FTC*, 570 F.2d 157 (7th Cir. 1977, supp. opinion Jan. 28, 1978).

gether with the 1975 Leavitt Study (CX 349) produced fairly consistent results which support that conclusion. Although they were not perfect surveys they were in general of the kind and quality normally used by business firms to help guide their market efforts. An analysis of the data pertaining to efficacy- and safety-related product attributes shows that consumers for some years have believed that Bufferin and Excedrin were superior to aspirin in those respects claimed by the advertisements. Thus these penetration/image studies confirm what common sense and experience suggest, namely, that Bristol-Myers' dissemination of the challenged advertising claims over a long period of time led to consumer images that Bufferin is faster and gentler than aspirin and Excedrin is faster and more effective than aspirin.

Next, the Commission has consistently rejected the argument that the image consumers may have about a product is the result of many and varied causative factors and that advertising cannot be singled out as the primary factor in the absence of empirical evience which establishes a causal relationship between advertisements and consumer images.[49] The remarkable correspondence between advertising claims and consumer images shown in this record is further indication that advertising played a significant role in creating or reinforcing those images.

With respect to the duration issue, the record as a whole supports the conclusion that the consumer images about Bufferin and Excedrin that have been found to exist will endure for some time and will tend to be reinforced either by subsequent advertising or by subsequent use.[50]

2. The Corrective Advertising Requirement

The basic rationale of corrective advertising is that a misleading product image, once created, is likely to endure unless

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49 See *e.g.*, *Warner-Lambert Co.*, *supra*, 86 F.T.C. at 1501-02, 1503 (1975), 562 F.2d at 762; *Walthum Instrument Co.*, 61 F.T.C. 1027, 1049 (1962), *aff'd*, 327 F.2d 427 (7th Cir. 1964), *cert. denied*, 377 U.S. 992 (1964).

50 *Cf. Warner-Lambert Co.*, *supra*, 86 F.T.C. at 1501-03, 562 F.2d at 762; *National Commission on Egg Nutrition* v. *FTC*, *supra*.

that image is unlearned by consumers through exposure to an appropriate corretive message for a sufficient time period. The Commission's Section 5 power to require corrective advertising in appropriate cases is not open to question. *Warner-Lambert Co., supra*; *National Commission on Egg Nutrition, supra*. Complaint counsel argue that the finding that some of respondents' advertisements contained an implied establishment claim of superior efficacy and safety and the finding that some consumers held corresponding superiority images about Bufferin and Excedrin requires a corrective advertising requirement. I am of the view that the corrective advertising requirement is a discretionary remedy and that considerations of fundamental fairness and equity are relevant, although in all cases the elimination of mistaken consumer images is the paramount consideration.

In this case, although the finding of an implied establishment claim in certain advertisements is supported by the record and is a fair inference, I am not persuaded that the record supports an inference that consumers have an *establishment* image or that such an inference is fair in the circumstances of this case. It is one thing to find an implied establishment claim in certain of respondents' advertisements and to require in future advertisements containing such establishment claims, an affirmative disclosure of the material fact that a substantial question exists. It is entirely another matter to find an implied establishment claim and require a corrective advertising saying essentially that the past establishment claims were false in cases where, as here, the claimed product performance characteristics (faster, stronger, or gentler) are not alleged to be false. Indeed the record contains substantial evidence which indicates that the superiority claims involved in this case, although not ''established,'' are based on sound pharmacological rationale and are not outright falsehoods. Furthermore, if a finding of ''establishment'' image among consumers is to be logically inferred from the fact of superiority images about Bufferin and Excedrin, the basis for doing so in this case is less than substantial, for the evidence of consumer images itself is less than overwhelming. Finally, as a practical matter

the disclosure requirements regarding the existence of aspirin in Bufferin and Exedrin as well as the existence of a substantial question in future advertisements will sufficiently inform consumers of the fact that Bufferin and Excedrin are aspirin-based products and that any comparative claim being made about them is not scientifically established, and by so doing may have the further effect of causing some consumers to modify accordingly their image of superiority of Bufferin and Excedrin. On balance, it is determined that on the basis of this record, corrective advertising directed to comparative images of Bufferin and Excedrin is not justified.[51]

With regard to the tension claim, there is evidence tending to show that consumers have a tension relief image about OTC headache tablets as a class and that Bristol-Myers' tension relief claims may have played a significant role in reinforcing them with respect to Bufferin and Excedrin, if not in creating them in the first place. However, in view of the fact that Bristol-Myers' tension relief claims ceased some ten years ago, a corrective advertising requirement directed to the tension reliever image appears unnecessary.

R. Relief

It is axiomatic that in Section 5 cases the Commission has the power and duty to fashion appropriate remedies which are reasonably calculated to prohibit the unlawful practices found to exist. *E.g.*, *Jacob Siegel Co. v. FTC*, 327 U.S. 608, 611-13

51 In theory a corrective advertisement provision may be justified on the basis of Complaint Paragraphs 9 and 10, for the reason that respondents' unqualified and misleading superiority claims made over many years played a significant role in creating and reinforcing corresponding consumer images of superiority of Bufferin and Excedrin over aspirin and that, in the absence of a clear corrective message in future advertisements, these images are likely to endure. However, the focus of complaint counsel's arguments in support of corrective advertising was placed upon "false establishment images." See CCM, at 209-11, 223-26, 239-40. In any event, although the evidence supports a finding that consumers held superiority images about Bufferin and Excedrin during the years 1967-70 and 1975, the evidence is not so clear and convincing as to support a finding that, but for a corrective message in every future advertisement, these images are likely to endure *after the offensive advertisements have ceased*. In my view, this case is clearly distinguishable from *Warner-Lambert*, where the cold-preventive image of Listerine was shown to be about three times as high as that of competitive products. 86 F.T.C. at 1503.

(1946); *FTC v. Ruberoid Co.*, 343 U.S. 470, 473 (1952); *FTC v. National Lead Co.*, 352 U.S. 419, 428-30 (1957). The remedy must have a reasonable relationship to the unlawful practice and be no broader than is reasonably necessary to remedy the violation. *Jacob Siegel Co. v. FTC*, *supra* at 613; *Beneficial Corp. v. FTC*, 542 F.2d 611, 619-20 (3d Cir. 1976). See also *Warner-Lambert Co. v. FTC*, 562 F.2d 749, 757-58 (D.C. Cir. 1977); *National Commission on Egg Nutrition v. FTC*, 570 F.2d 157, 164 (7th Cir. 1977).

1. The Reasonable Basis Provision Is Justified

Part I of the Order would prohibit simple and non-comparative efficacy or safety claims or recommendation claims that are not supported by a reasonable basis. This prohibition is based on the findings that Bristol-Myers made tension reliever claims for Bufferin, Excedrin and Excedrin P.M. and endorsement or recommendation claims for Bufferin without adequate substantiation. Although the tension reliever claims ceased in 1970, the provision is necessary to prevent a renewal of that claim as well as any other claims concerning any non-prescription drug product not supported by a reasonable basis.

Inclusion of all OTC drug products in the reasonable basis requirement provision is appropriate in this case. Bristol-Myers appears to have been involved in a number of Section 5 proceedings which resulted in cease and desist orders, consent orders or stipulations involving misrepresentation of a number of OTC drug and cosmetic products.[52] In *Grove Laboratories*,

52 See *Bristol-Myers Co.*, 36 F.T.C. 707 (1943) (efficacy claim of "Sal Hepatica"); *Bristol-Myers Co.*, 46 F.T.C. 162 (1949), *aff'd*, 185 F.2d 58 (4th Cir. 1950) (therapeutic claim of a toothpaste); *Bristol-Myers Co.*, 47 F.T.C. 1441 (1950) (efficacy claim of "Resistab"); *Grove Laboratories, Inc.*, 71 F.T.C. 822 (1967), *rev'd in part*, 418 F.2d 489 (5th Cir. 1969) (efficacy claims of a hemorrhoidal preparation); *Bristol-Myers Co.*, 74 F.T.C. 780 (1968) (safety claim of Bufferin). In addition, Bristol-Myers has entered into six stipulations regarding the advertising of its products. 24 F.T.C. 1546 (1937) (relating to health claims for "Vitalis"); 24 F.T.C. 1546 (1937) (relating to health claims for Ipana toothpaste); 24 F.T.C. 1558 (1937) (relating to health claims for "Sal Hepatica," a laxative); 25 F.T.C. 1626 (1937) (relating to claims for "Minit-Rub," an alleged cold remedy); 27 F.T.C. 1602 (1938) (relating to skin claims for "Ingram's Milkweed Cream"); 27 F.T.C. 1609 (1938) (relating to health claims for "Ingram's Shaving Cream").

Grove (owned by Bristol-Myers) was found to have falsely represented the therapeutic effect of a hemorrhoid preparation, and was ordered to cease misrepresenting the ability of any "drug" to prevent or treat hemorrhoids. The Commission found that it was obligated to include all drug products in the order, saying,

> [W]e are convinced that we would be derelict in our responsibilities if we were to limit the prohibitions of the order against false representations solely to hemorrhoidal preparations having the same or similar ingredients. The ease with which such orders can be avoided has been amply demonstrated by the Commission's experience with this respondent alone. We are equally convinced that it is essential that this order also "fence this respondent in" in connection with all of its future advertising of drug preparations. It is our judgment that in the circumstances of this case and of this respondant, it is essential that the order which we are entering cover all drug products sold by respondent. 71 F.T.C. at 847-48.

The Commission's order also broadly prohibited respondent from "misrepresenting the efficacy of any drug" (418 F.2d at 497). The Fifth Circuit reversed the all-drugs-products order coverage on the grounds that it was a "close question" whether the past history of Grove and Bristol-Myers warranted broad product coverage. It is my view that now is the time to place Bristol-Myers under a broad proscription with respect to all OTC drug products marketed by it. Furthermore, the proscription here is narrower and is related to the particular types of claims involved in this case.

2. *Substantial Question Disclosure Requirement Should be Limited to OTC Analgesic Products*

Part III A of the Order would prohibit Bristol-Myers from making comparative efficacy and safety claims of any OTC internal analgesic products without disclosing the existence of a substantial question unless the claim is not scientifically established. The requirement for two or more "adequate and well-controlled" clinical investigations are based on the FDA regulation which sets forth similar criteria necessary to provide

"substantial evidence" of efficacy for new drugs (21 CFR § 331.lll(a)(5)(ii) and § 330.10(a)(4)(ii), with certain modifications. The FDA regulation has been modified to reflect the facts that (1) this case involves comparative efficacy and safety, and (2) this case involves only OTC drug products. In this respect, I have adopted complaint counsel's proposed order provisions and hereby subscribe to the reasons explained in complaint counsel's Memorandum (CM, 193-96).

With respect to the product scope of this provision I am now of the view that the substantial question disclosure should be limited to OTC internal analgesic products for the reason that the record provides an insufficient basis for concluding that the implied establishment claim/substantial question theory discussed in this case would be equally valid for all OTC drug products. There is some evidence from which it can be inferred that the considerations discussed in connection with the establishment/substantial question issue related to OTC analgesic products may be equally valid with respect to all OTC drug products. For example, the FDA's requirements for clinical demonstration of efficacy and safety by two or more well-controlled studies apply to all new drugs. In establishing the monograph procedures for certain classes of OTC drugs, including OTC analgesics, the FDA incorporated similar standards for labeling purposes.

However, in the final analysis the establishment/substantial question theory in this case is essentially anchored in the reasonable basis doctrine. What constitutes a reasonable basis for an advertising claim is a question of fact to be determined on a case-by-case basis and depends on, among other things, the nature of the product and the type of claim involved.[53] Although it is eminently plausible to conclude that the essential rationale of the substantial question disclosure requirement with respect to headache tablets will be valid for OTC drug products of other classes, I am not persuaded that this adjudicative record involving OTC internal analgesic products provides a sufficient basis for extending the establishment/substantial question disclosure provision of the Order to

53 *Pfizer*, 81 F.T.C. at 64, 66-67.

all OTC drug products. For the same reasons, the fencing-in argument, valid with respect to the reasonable basis provision of the Order, is inappropriate with respect to the establishment/substantial question disclosure provision.[54]

S. Liability of Advertising Agencies

The law is well-settled that an advertising agency may be held liable for false advertising if it "actually participated in the deception. . . In order to be held a participant in such deception, the agency must know or have reason to know of the falsity of the advertising." *Doherty, Clifford, Steers and Shenfield, Inc. v. F.T.C.*, 392 F.2d 921, 918 (6th Cir. 1968); also *Carter Products, Inc. v. F.T.C.*, 323 F.2d 523, 534 (5th Cir. 1963); *ITT Continental Baking Co., Inc.* 83 F.T.C. 865 (1973).

In determining liability, the agency will be strictly held to know what claims are made in advertisements. *In re Merck & Co.*, 69 F.T.C. 526, 559 (1966), *aff'd*, 392 F.2d 921 (6th Cir. 1968). *ITT Continental, supra*. Since it is undisputed that Bates and Young & Rubicam actively participated in the creation and dissemination of the challenged advertisements for Bufferin, Excedrin and Excedrin P.M., the remaining issues regarding their respective liability are whether each knew or should have known that the advertisements they disseminated were false due to failure to disclose material facts of the presence of aspirin and the existence of a substantial question in the medical scientific community concerning the validity of the "establishment" claims regarding these products.

Complaint counsel argue that both respondents' absolute and comparative efficacy (and related) claims for Bufferin, Excedrin, and Excedrin P.M. were false because, having represented these claims as being "established" by scientific evidence Ted Bates knew or should have known that the data supporting the claims were subject to "substantial question"

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54 This view represents a modification of my views expressed in the Initial Decision in *American Home Products Corporation*, Docket No. 8918, filed 9/1/78, regarding the propriety of an "all drug products" coverage with respect to a similar disclosure requirement in the order therein.

among experts and that the existence of such substantial question was a material fact which should have been disclosed to consumers. A similar allegation is made with respect to Bufferin's Doctors Recommend'' advertisements, the ''antidepressant'' claims imputed to Excedrin, and the ''mild sedative claims imputed to Excedrin P.M. Complaint counsel also argue that the failure of both respondents to include the presence of aspirin in these analgesics was false because both advertising agencies knew, or should have known, that since aspirin may cause undesirable side effects in certain users, implicit promotion of these analgesics as containing ingredients other than aspirin and failure to disclose the presence of aspirin was false advertising by virtue of the fact that the presence of aspirin is material fact, knowledge of which may cause some consumers to change their purchase decisions.

It is my determination that the record as a whole: (1) fails to support allegations in the complaint relative to the imputed ''antidepressant'' and ''mild sedative'' claims for Excedrin and Excedrin P.M. respectively (2) supports the complaint allegations that the failure to disclose the presence of aspirin in all three analgesics constituted knowingly false advertising relative to the imputed claims for Bufferin, Excedrin and Excedrin P.M. that the analgesic ingredient in these products was something other than aspirin for which respondent advertising agencies should be held liable; and (3) supports the conclusion that both respondents' good faith reliance on the substantiation information with respect to the comparative efficacy and safety claims for Bufferin, Excedrin, and Excedrin P.M., as well as the tension relief claims was reasonable under the circumstances.

With respect to the tension relief claim, although the dated medical literature on which Bristol-Myers relied on did not constitute a reasonable basis for Bristol-Myers which was in a position to evaluate the nature and reliability of the purported substantiation, I am unable to conclude that it was not reasonable for the advertising agencies to have relied on Bristol-Myers Medical Department's judgment as to medical-scientific substantiation for the claim. In other words, what may not

be a reasonable basis for a medical-scientific claim for a drug manufacturer may be a reasonable basis for an advertising agency which relied in good faith on the client drug manufacturer's judgment regarding the adequacy of substantiation, unless the purported substantiation was unreliable on its face. However, in view of the specific findings made herein with regard to the inadequacy of medical substantiation for the tension relief claim, the advertising agencies should be prohibited in the future from continuing to make such claims until the day something more than what was relied on by respondents in this case is forthcoming.

With respect to advertising agency's liability under the establishment/substantial question theory it is my determination that the same standards applicable to drug manufacturing firms are not appropriate for advertising agencies in this case.

Here, as in my Initial Decision in *American Home Products*, Docket No. 8918, dated 9/1/78 (p. 225), respondents are found to have acted reasonably in relying in good faith on the substantiation data provided by Bristol-Myers. As the record in this case amply demonstrates, scientific analysis or verification of the accuracy of clinical data is a highly complex technical process, one for which the two advertising agencies are not and may not reasonably be expected to be equipped. Even where complaint counsel have shown the advertising agencies to have been aware of some questions concerning the validity of their unqualified representations, respondents were not obligated to perform statistical or clinical analyses of their representations to determine the "substantiality" of the question or its "materiality." I reiterate my conclusions in *American Home Products*:

> This is not a case where the disparity between the advertising representations and the substantiation information is so great as to preclude a conclusion that the advertisements were conceived through reasonable reliance on the assurances of the manufacturer that the claim is true or has a reasonable basis. *Cf. Standard Oil Co. of California*, 84 F.T.C. 1401, 1474-75 (1974). Clyne [adver-

tising agency] cannot be reasonably charged with the duty to conduct an independent investigation that the claim is scientifically established in the sense that there existed two or more well-controlled clinical demonstrations in support of the claim. In these circumstances Clyne's good faith reliance on American Home's assurances, as embodied in CX 304, was reasonable.

* * *

CONCLUSIONS OF LAW

1. The Federal Trade Commission has the jurisdiction over the advertising of Bufferin Excedrin and Excedrin P.M. under Section 5 of the Federal Trade Commission Act.

2. Respondents' false and misleading advertising representations as alleged in the Complaint and as herein found to have been made with the exception of Paragraphs 7A(3), 9A(3), 12C and 14A (as relates "twice as strong" claim), have had and now have the capacity and tendency to mislead consumers into the mistaken belief that the said representations are true and into purchasing substantial quantities of Bufferin, Excedrin and Excedrin P.M. by reason of said mistaken belief. In the absence of an appropriate cease and desist order, including appropriate affirmative disclosure requirements, consumers will continue to be misled by respondents' advertisements that certain advertising representations being made regarding efficacy or safety of said products are supported by medical-scientific evidence generally accepted by the scientific community as establishing such propositions or have adequate substantiation.

3. The acts and practices of respondents as found herein were and are prejudicial and injurious to the public and constitute unfair methods of competition and unfair and deceptive acts in commerce in violation of Sections 5 and 12 of the FTC Act.

4. The Complaint is hereby dismissed: (A) as to all respondents insofar as it relates to the advertising representations alleged in Complaint Paragraphs 7A(3), 9A(3), 12C and 14A (as relates to "Bufferin is twice as strong as aspirin" claims);

and (B) as to Ted Bates & Company and Young & Rubicam, Inc. insofar as it relates to the allegations in "Complaint" paragraphs 10; 11, 15 and 16.

5. The accompanying order is necessary and appropriate for the purpose of prohibiting the continuation of the proscribed acts and remedying the injury and unfairness to the consuming public.

ORDER

I.

IT IS ORDERED that respondent Bristol-Myers Company, a corporation, its successors and assigns and respondent's officers, agents, representatives and employees directly or through any corporation, subsidiary, division or other device, in connection with the labeling, advertising, offering for sale, sale or distribution of any nonprescription drug in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from:

A. Representing, directly or by implication, that such product relieves nervousness, tension, anxiety or depression or will enable persons to cope with the ordinary stresses of everyday life; or

B. Making any statements or representations, directly or by implication, concerning the effectiveness or freedom from side effects of such product; or

C. Representing that any group, body or organization endorses or recommends such product;

unless at the time such statement or representation is made respondent has a reasonable basis for such statement or representation, which shall consist of competent and reliable scientific evidence.

II.

IT IS FURTHER ORDERED that respondent Bristol-Myers Company, a corporation, its successors and assigns and respondent's officers, agents, representatives and employees directly or through any corporation, subsidiary, division or other

device, in connection with the labeling, advertising, offering for sale, sales or distribution of Bufferin, Excedrin, Excedrin P.M. or any other nonprescription drug in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act do forthwith cease and desist from:

A. Representing that such product contains any ingredient, or combination of ingredients which is unusual, special or exclusive when such ingredient, or combination of ingredients, is available in other nonprescription analgesic products.

B. Referring, directly or by implication to aspirin, caffeine or any commonly known ingredient by any word or words without disclosing the common, or usual, name of such ingredient.

C. Failing to disclose in the advertising of any nonprescription drug product intended for internal use, the presence of aspirin when such product contains aspirin.

D. Misrepresenting in any manner any test study or survey or any results thereof.

III.

IT IS FURTHER ORDERED that respondent Bristol-Myers Company, its successors and assigns and respondent's officers, agents, representatives and employees, directly or through any corporation, subsidiary, division or other device, in connection with the labeling, advertising, offering for sale, sale or distribution of Bufferin, Excedrin, Excedrin P.M., or any other nonprescription internal analgesic product, in or affecting commerce as "commerce" is defined in the Federal Trade Commission Act, do forthwith cease and desist from:

A. Representing, directly or by implication, that a claim concerning the comparative effectivensss or comparative freedom from side effects of such product has been established unless such representation has been established by two or more adsquate and well-controlled clinical inyestigations conducted by independent experts

qualified by training and experience to evaluate the effectiveness and comparative effectiveness or comparative freedom from side effects of the drugs involved, on the basis of which it could fairly and responsibly be concluded by such experts (1) that the drug will have the comparative effectiveness or comparative freedom from side effects it is represented to have, and (2) that such comparative effectiveness or comparative freedom from side effects is demonstrated by methods of statistical analysis, and with levels of confidence, that are generally recognized by such experts. At least one of the adequate and well-controlled clinical investigations to evaluate the comparative effectiveness of the drug shall be conducted on any pain or condition referred to, directly or by implication; or, if no specific pain or condition is referred to, then the adequate and well-controlled clinical investigations shall be conducted on at least two types of pain or conditions for which the drug is effective. To provide the basis for the determination whether any clinical investigation is "adequate and well-controlled," the plan or Protocol for the investigation and the report of the results must include the following:

1. A clear statement of the objective of the investigation.

2. A method of selection of the subjects that:

a. Provides adequate assurance that they are suitable for the Purposes of the investigation, and diagnostic criteria of the condition to be treated (if any);

b. Assigns the subjects to the test groups in such a way as to minimize bias;

c. Assures comparability in test and control groups of pertinent variables, such as age, sex, severity, or duration of disease or condition (if any), and use of drugs other than the test drugs.

3. An explanation of the methods of observation and recording of results, including the variables measured, quantitation, assessment of any subject's response and steps taken to minimize bias on the part of the subject and observer.

4. A comparison of the results of treatments or diagnosis with a control in such a fashion as to permit quantitative evaluation. The precise nature of the control must be stated and an explanation given of the methods used to minimize bias on the part of the observers and the analysts of the data. The investigation must be conducted double-blind, and methods of double-blinding must be documented. In addition, the investigation must contain a placebo control to permit comparison of the results of use of the test drugs with an inactive preparation designed to resemble the test drugs as far as possible.

5. A summary of the methods of analysis and an evaluation of data derived from the study, including any appropriate statistical methods.

B. Making any statement or representation directly or by implication, concerning the comparative effectiveness or comparative freedom from side effects of such product, when there exists a substantial question, recognized by experts qualified by scientific training and experience to evaluate the efficacy and safety of such drug product, as to the validity of any such statement or representation, unless respondent discloses the existence of such substantial question by including in the same advertisement a clear and conspicuous disclosure statement conforming to the following:

1. The disclosure statement regarding comparative efficacy [and/or safety] for Bufferin should state "Bufferin has not been proven to be a faster pain reliever [and/or gentler to the stomach] than aspirin," or comprise such other statement approved by the Federal Trade Commission in advance or as respondent can demonstrate (based on consumer sur-

veys whose design is adequate and previously approved by the Federal Trade Commission) will convey the same message to consumers.

2. The disclosure statement regarding comparative speed [and/or efficacy] for Excedrin should state "Excedrin has not been proven to be a faster [and/or stronger] pain reliever than aspirin," or comprise such other statement determined and approved as set forth in 1 herein above.

3. The disclosure statemant regarding comparative efficacy for Excedrin P.M. should state "Excedrin P.M. has not been proven to be stronger pain reliever than aspirin" or comprise such other statement determined and approved as set forth in 1 herein above.

4. In print advertisements, the disclosure shall be displayed in type size which is at least the same size as that in which the principal portion of the text of the advertisement appears and shall be separated from the text so that it can be readily noticed.

5. In television advertisements the disclosure shall be presented simultaneously in both the audio and video portions. During the audio portion of the disclosure in television and radio advertisements, no other sounds, including music shall occur. Each such disclosure shall be presented in the language principally employed in the advertisement.

IV.

IT IS FURTHER ORDERED that respondent Ted Bates & Co., Inc., a corporation, its successors and assigns, and respondent's officers, agents, reprssentatives and employees directly or through any corporation, subsidiary, division or other device, in connection with the labeling, advertising, offering for sale, sale or distribution of Bufferin in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act do forthwith cease and desist from:

A. Representing, directly or by implication, that Bufferin will not upset a person's stomach, unless respondent has a reasonable basis for such representation consisting of competent and reliable scientific evidence;

B. Representing, directly or by implication, that Bufferin will relieve nervous tension, anxiety or irritability or will enable persons to cope with the ordinary stresses of everyday life unless respondent has a reasonable basis for such representations;

C. Referring to the ingredient aspirin by any word or words other than "aspirin";

D. Failing to disclose, clearly and conspicuously, that the product contains aspirin; or

E. Representing, directly or by implication, that physicians recommend Bufferin more than any other nonprescription internal analgesic product, unless respondent has a reasonable basis for such representation consisting of competent and reliable surveys of physicians.

V.

IT IS FURTHER ORDERED that respondent Young & Rubicam, Inc., a corporation, its successors and assigns, and respondent's officers, agents, representatives and employees directly or through any corporation, subsidiary, division or other device, in connection with the labeling, advertising, offering for sale, sale or distribution of Excedrin or Excedrin P.M. in or affecting commerce, as "commerce" is defined in the Federal Trade Commission Act do forthwith cease and desist from:

A. Representing, directly or by implication, that Excedrin or Excedrin P.M. will relieve tension, nervousness, anxiety or irritability or will enable persons to cope with the ordinary stresses of everyday life unless respondent has a reasonable basis for such representations.

B. Referring to the ingredient aspirin in Excedrin or Exedrin P.M. by any other word or words other than "aspirin";

C. Failing to disclose, clearly and conspicuously, that the products contain aspirin; or

D. Representing, directly or by implication, that physicians recommend such products, unless at the time of such representations respondent has a reasonable basis for such representation consisting of competent and reliable surveys of physicians.

VI.

IT IS FURTHER ORDERED that respondents herein shall notify the Commission at least thirty (30) days prior to any proposed change in their respective corporate respondent such as dissolution, assignment or sale resulting in the emergence of a successor corporation, the creation or dissolution of subsidiaries or any other change in their respective corporation which may affect compliance obligations under this Order.

VII.

IT IS FURTHER ORDERED that the respondents herein shall within sixty (60) days after service of this Order upon them, file with the Commission a written report setting forth in detail the manner and form in which they have complied or intend to comply with this Order.

Paragraphs Seven A(3), Nine A(3), Twelve C and Fourteen A as relates to "Bufferin is twice as strong as aspirin" claim, of the Complaint are hereby dismissed as to all respondents. Paragraphs Ten, Eleven, Fifteen and Sixteen of the Complaint are hereby dismissed as to Ted Bates & Company, Inc. and Young & Rubicam, Inc.

Montgomery K. Hyun
Administrative Law Judge

September 28, 1979

Complaint Counsel's Revised Answering Brief

UNITED STATES OF AMERICA
BEFORE FEDERAL TRADE COMMISSION

Docket No. 8917

In the Matter of

BRISTOL-MYERS COMPANY,
a corporation,

TED BATES & COMPANY, INC.,
a corporation, and

YOUNG & RUBICAM, INC.,
a corporation.

COMPLAINT COUNSEL'S REVISED ANSWERING BRIEF

W. Benjamin Fisherow
Ira Nerken
Leslie Fax
Randell Ogg

Counsel Supporting
the Complaint

Thomas J. Donegan, Jr.
Assistant Director for
Food and Drug Advertising

Rae Ellen Alperstein
Research Analyst

Albert H. Kramer
Director,
Bureau of Consumer Protection

April 4, 1980

* * *

D. Part IIA of the Order is Justified

Although the complaint alleged Paragraph 23) and the ALJ found (F. 359-361) that respondent represented that Excedrin P.M. contained a unique ingredient, respondent now claims that all it represented was that Excedrin P.M.'s *formula* was unique. (BMAB, p. 34). The advertisements themselves refute respondent's position. Examples such as CXs 213, 214, 215, 218, 224 and 242 explicitly tell consumers that Excedrin P.M. combines pain relief "with a special nighttime ingredient that gently helps you sleep." Dr. Ross testified that this claim would be understood, and reasonably so, by consumers as a claim that the product's sleep-inducing ingredient was unique (Tr. 7155-56). This is false, as the ALJ found, because the "unique" ingredient in Excedrin P.M., methapyriline fumarate, is an antihistamine available in other OTC medications like Cope (F. 629). Given the falsity of this "uniqueness" claim, Part IIA of the order which prohibits such a false claim in the future is justified.

* * *

CERTIFICATE OF SERVICE

I, Kenneth A. Plevan, a member of the Bar of this Court and counsel for Petitioner herein, hereby certify that on this 23rd day of October, 1984, the "Appendix to Petition for a Writ of Certiorari to the United States Court of Appeals for the Second Circuit" was served upon all parties required to be served by hand delivery of three copies of same to:

1) Office of the General Counsel
   Federal Trade Commission
   Washington, D.C. 20580

2) Solicitor General
   Department of Justice
   Washington, D.C. 20530

/s/ KENNETH A. PLEVAN

Kenneth A. Plevan
Skadden, Arps, Slate, Meagher & Flom
919 Third Avenue
New York, New York 10022